201-15982

I U C L I D

Data Set

Existing Chemical	:	ID: 108-46-3
CAS No.	:	108-46-3
EINECS Name	:	resorcinol
EC No.	:	203-585-2
TSCA Name	:	1,3-Benzenediol
Molecular Formula	:	C6H6O2

Producer related part

Company	:	Indspec Chemical Corporation
Creation date	:	03.11.2003

Substance related part

Company	:	Indspec Chemical Corporation
Creation date	:	03.11.2003
Status	:	
Memo	:	
Printing date	:	13.09.2005
Revision date	:	
Date of last update	:	13.09.2005
Number of pages	:	123
Chapter (profile)	:	
Reliability (profile)	:	
Flags (profile)	:	

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	
Name	:	INDSPEC Chemical Corporation
Contact person	:	
Date	:	
Street	:	411 Seventh Avenue, Suite 300
Town	:	15219 Pittsburgh, PA
Country	:	United States
Phone	:	412-765-1200
Telefax	:	412-765-0439
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

13.11.2003

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name	:	Resorcinol
Smiles Code	:	c1(O)cc(O)ccc1
Molecular formula	:	C6H6O2
Molecular weight	:	110.11
Petrol class	:	
Reliability	:	(1) valid without restriction

27.04.2004

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	
Substance type	:	organic
Physical status	:	solid
Purity	:	
Colour	:	White-slightly colored flake or powder
Odour	:	Phenolic

27.04.2004

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

1,3-Benzenediol 1,3 Dihydroxybenzene

25.03.2004

Resorcin

27.04.2004

Resorcinol

27.04.2004

1.3 IMPURITIES

Purity	:	typical for marketed substance
CAS-No	:	
EC-No	:	
EINECS-Name	:	
Molecular formula	:	
Value	:	
Remark	:	The impurities present depend on the manufacturing process. Sulfonation Fusion Process has catechol and phenol as major impurities

27.04.2004

1.4 ADDITIVES

1.5 TOTAL QUANTITY

1.6.1 LABELLING

Labelling	:	as in Directive 67/548/EEC
Specific limits	:	yes
Symbols	:	Xn, N, ,
Nota	:	C, ,
R-Phrases	:	(22) Harmful if swallowed (36/38) Irritating to eyes and skin (50) Very toxic to aquatic organisms
S-Phrases	:	(61) Avoid release to the environment. Refer to special instructions/Safety data sets
Remark	:	Labelling per U.S. Standards (ANSI Z129.1): Danger! Corrosive To The Eyes. Harmful If Swallowed. May Cause Skin Irritation. May Cause Allergic Skin Reaction. May be Harmful If Absorbed Through The Skin. Ingestion May Injure The Blood, Gastrointestinal Tract, Spleen, Liver, Kidneys, Lungs, Nervous System, Thyroid, and Skin.

27.04.2004

1.6.2 CLASSIFICATION

Classified	:	as in Directive 67/548/EEC

Class of danger : dangerous for the environment
R-Phrases : (50) Very toxic to aquatic organisms
Specific limits :

11.11.2003

Classified : as in Directive 67/548/EEC
Class of danger : harmful
R-Phrases : (22) Harmful if swallowed
Specific limits :

27.04.2004

Classified : as in Directive 67/548/EEC
Class of danger : irritating
R-Phrases : (36/38) Irritating to eyes and skin
Specific limits :

14.01.2004

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : industrial
Category : Chemical industry: used in synthesis

11.11.2003

Type of use : industrial
Category : Polymers industry

11.11.2003

Type of use : industrial
Category : Textile processing industry

11.11.2003

Type of use : use
Category : Adhesive, binding agents

27.04.2004

Type of use : use
Category : Cosmetics

Remark : The use includes funical creams/lotions, hair dyes
27.04.2004

Type of use : use
Category : Intermediates

Remark : Intermaediates for light screening agent, flame retardants, agricultural chemicals, explosive primers dye stuffs.

27.04.2004

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : TLV (US)
Limit value : 45 mg/m3
Short term exposure limit value
Limit value : 90 mg/m3
Time schedule : 15 minute(s)
Frequency : times

14.01.2004 (2)

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

Remark : Options for disposal:
Disposal methods include complete incineration, land (soil) farming and decomposition in activated sludge type wastewater treatment plants.

02.06.2004 (125)

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value	:	109 - 111 °C
Decomposition	:	no, at °C
Sublimation	:	yes
Method	:	other
Year	:	No data
GLP	:	no data
Test substance	:	Other TS: see remark
Source	:	The Merck Index
Test substance	:	Pressed flake resorcinol
Reference	:	Thermophysical properties of resorcinol. A report to INDSPEC Chemical Corp. by R.E Taylor and H. Groot
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

14.09.2005 (93) (125)

2.2 BOILING POINT

Value	:	280 °C at
Decomposition	:	No data
Method	:	other: no data
Year	:	No data
GLP	:	no data
Test substance	:	other TS: see remark
Source	:	The Merck Index
Test substance	:	Resorcinol (Cas No. 108-46-3) Purity not given
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

14.09.2005 (93)

Value	:	276.7 °C at 1013 hPa
Decomposition	:	yes
Method	:	other
Year	:	1998
GLP	:	No data
Test substance	:	Other TS:
Test substance	:	Ppressed flake resorcinol
Reference	:	Thermophysical properties of resorcinol. A report to INDSPEC Chemical Corp. by R.E Taylor and H. Groot
Reliability	:	(2) valid with restrictions

14.09.2005 (125)

2.3 DENSITY

Type	:	density
Value	:	1.272 at °C
Method	:	other: no data
Year	:	No data
GLP	:	no data
Test substance	:	other TS: see remark
Source	:	The Merck Index

Test substance : Resorcinol (Cas no. 108-46-3) Purity not given
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
26.05.2004 (93)

Type : density
Value : 1.227 at °C
Method : other
Year : 1998
GLP : no data
Test substance : Other TS:

Test substance : Pressed flake resorcinol
Reference : Thermophysical properties of resorcinol. A report to INDSPEC Chemical Corp. by R.E Taylor and H. Groot
Reliability : (2) valid with restrictions
14.09.2005 (125) (126)

Type : bulk density
Value : 1.292 g/cm³ at 20 °C
Method : other
Year : No data
GLP : No data
Test substance : No data

Reliability : (4) not assignable
14.09.2005 (75)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : .01466 hPa at 25 °C
Decomposition : No data
Method : other (calculated)
Year : 2004
GLP : No data
Test substance : other TS: see remark

Method : MPBPWIN v1.30 vapor pressure estimations (modified grain method)
Result : 0.011 mm Hg (0.01466 hPa) @ 25°C
Test substance : Resorcinol (Cas no. 108-46-3)
Reliability : (2) valid with restrictions
14.09.200 (128)

Value : .00027 hPa at 25 °C
Decomposition : No data
Method : other (measured)
Year : No data
GLP : No data
Test substance : No data

Reliability : (4) not assignable
14.09.2005 (37)

Result : 1.33 hPa @ 108.4°C
6.65 hPa @ 138°C

13.3 hPa @ 152.3°C
53.2 hPa @ 185.3°C
133 hPa @ 210°C
266 hPa @ 230.8°C

Reference : Thermophysical properties of resorcinol. A report to INDSPEC Chemical Corp. by R.E Taylor and H. Groot
Reliability : (2) valid with restrictions
13.09.2005 (125)

2.5 PARTITION COEFFICIENT

Partition coefficient : Ca 6.3
Log pow : = .8 at 35 °C
pH value : No data

Result : 0.93 log Pow @ 20°C; 0.97 log Pow @ 15 °C
Reliability : (2) valid with restrictions
14.09.2005 (5)

Partition coefficient : Ca. 10.7
Log pow : 1.03 at °C
pH value : No data
Method : other (calculated): EPIWIN v3.01
Year : 2004
GLP : No data
Test substance : No data

Source : EPI Summary (V3.01)
14.09.2005 (128)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water
Value : 85710 mg/l at 25 °C
pH value : No data
concentration : at °C
Temperature effects : No data
Examine different pol. : No data
pKa : at 25 °C
Description : of high solubility
Stable : No data
Deg. product : No data
Method : other: EPIWIN v 3.01
Year : 2004
GLP : No data
Test substance : other TS: see remark

Method : Water solubility Estimate from Log KOW (WSKOW v1.33)
Source : EPI summary (v3.01)
Test substance : Resorcinol (Cas No. 108-46-3)
Reliability : (2) valid with restrictions
14.09.2005 (128)

Solubility in : Water
Value : at °C
pH value : No data
concentration : at °C
Temperature effects : No data

Examine different pol.	:	No data
pKa	:	at 25 °C
Description	:	No data
Stable	:	No data
Remark	:	Equivalent to 1.11E +7 mg/l at 20°C
Result	:	One gram dissolves in 0.9ml water, 0.2ml dissolves in 0.9 ml water, 0.2 ml water at 80°C
Reliability	:	(2) valid with restrictions

14.09.2005 (93)

Solubility in	:	Water
Value	:	= 58.4 vol% at 20 °C
pH value	:	= 4.5
concentration	:	10 vol% at 23 °C
Temperature effects	:	No data
Examine different pol.	:	No data
pKa	:	9.15 at 25 °C
Description	:	soluble (1000-10000 mg/L)
Stable	:	No data
Deg. product	:	No data
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Result	:	2290 g/l @ 30 °C; 5000 g/l @ 80°C
Reliability	:	(1) valid without restriction

14.09.2005 (82) (87)

Solubility in	:	Water
Value	:	= 1400 g/l at 20 °C
pH value	:	= 4.4
concentration	:	55 g/l at 20 °C
Temperature effects	:	No data
Examine different pol.	:	No data
pKa	:	at 25 °C
Description	:	No data
Stable	:	No data
Reliability	:	(2) valid with restrictions

14.09.2005 (56)

Solubility in	:	Water
Value	:	= 1290 g/l at 30 °C
pH value	:	No data
concentration	:	No data
Temperature effects	:	No data
Examine different pol.	:	No data
pKa	:	No data
Description	:	No data
Stable	:	No data
Remark	:	pKa = 11.32 @ 30°C
Reliability	:	(2) valid with restrictions

14.09.2005 (86)

Solubility in	:	Organic Solvents
Value	:	No data
pH value	:	No data
concentration	:	No data
Temperature effects	:	No data

Examine different pol.	:	No data
pKa	:	No data
Description	:	No data
Stable	:	No data
Remark	:	Solubility in acetone = 67 wt % @ 20°C and 75 wt % @ 60°C Solubility in ethanol = 61% wt % @ 20°C and 73% wt % @ 60°C Solubility in benzene = 2% wt % @ 20°C and 14% wt % @ 60°C
Reference	:	Thermophysical properties of resorcinol. A report to INDSPEC Chemical Corp. by R.E Taylor and H. Groot
Reliability	:	(2) valid with restrictions

14.09.2005 (125)

Solubility in	:	Water
Value	:	58 at 20 °C
pH value	:	No data
concentration	:	No data
Temperature effects	:	No data
Examine different pol.	:	No data
pKa	:	No data
Description	:	No data
Stable	:	No data
Result	:	53 wt% @ 20°C 83 wt% @ 60°C
Reference	:	Thermophysical properties of resorcinol. A report to INDSPEC Chemical Corp. by R.E Taylor and H. Groot
Reliability	:	(2) valid with restrictions

14.09.2005 (125)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value	:	= 127 °C
Type	:	closed cup
Method	:	other
Year	:	No data
GLP	:	No data
Test substance	:	No data
Method	:	ASTM D-93-97; closed cup
Reference	:	Thermophysical properties of resorcinol. A report to INDSPEC Chemical Corp. by R.E Taylor and H. Groot
Reliability	:	(2) valid with restrictions

14.09.2005 (125)

2.8 AUTO FLAMMABILITY

Value	:	= 608 °C at
Remark	:	This is auto ignition temperature
Reference	:	Thermophysical properties of resorcinol. A report to INDSPEC Chemical Corp. by R.E Taylor and H. Groot
Reliability	:	(2) valid with restrictions

13.09.2005 (45) (125)

2.9 FLAMMABILITY

Result	:	other
Method	:	other
Year	:	No data
GLP	:	No data
Test substance	:	No data
Remark	:	Flammable limit 1.4% by volume in air @ 200°C

14.09.2005 (91)

2.10 EXPLOSIVE PROPERTIES

Result	:	other
Method	:	other
Year	:	1997
GLP	:	no data
Test substance	:	no data
Method	:	BS 5958: Part 1: 1991 Control of Undesirable Static ElectricityVDI Forschritt-Berichte Reihe 3: Verfahrenstecknik Nr 134 ISO Explosion Protection Systems Part 1: Determination of Explosion Indices of Combustible Dusts in Air; ISO 6184/1 ISO Geneva (1985)
Remark	:	Minimum ignition temperature measured for resorcinol dust was reported at 3 mj at dust concentration of 8 kg/m³. The deflagration index reported for resorcinol dust was 134 which is a dust classification of St-1.
Reliability	:	(2) valid with restrictions

26.05.2004 (101)

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

Remark	:	Henry's Law constant: 8.1 x 10E-11 atm-cu m/mole @ 25°C 2.1 x 10E-6 Pa-cu m/mole @ 20°C Koc: estimated at 2 to 65 measured at 10.36 with water solubility of 1230 g/l and log Kow of 0.80.

13.11.2003 (78)

3.1.1 PHOTODEGRADATION

DIRECT PHOTOLYSIS
Halflife t1/2 : 38.5 minute(s)
Degradation : % after
Quantum yield : No data
INDIRECT PHOTOLYSIS
Sensitizer : No data
Conc. of sensitizer : No data
Rate constant : .00000000020028 $cm^3/(molecule*sec)$
Degradation : 50 % after 0 day(s)
Deg. product : No data
Method : Other (calculated)
Year : 2004
GLP : No data
Test substance : other TS

Method : EPIWIN v3.01 using AopWin v1.88
Source : EPI summary (V3.01)
Test substance : Resorcinol (Cas No. 108-46-3) No purity given
Reliability : (2) valid with restrictions
14.09.2005 (128)

Type : air
Light source : Sun light
Light spectrum : No data
Relative intensity : No data
Spectrum of substance : lambda (max, >295nm) : 274 nm
epsilon (max) : 2000
epsilon (295) :

DIRECT PHOTOLYSIS
Halflife t1/2 : = 100 hour(s)
Degradation : No data
Quantum yield : .03
INDIRECT PHOTOLYSIS
Sensitizer : OH
Conc. of sensitizer : 500000 $molecule/cm^3$
Rate constant : = .00000000002 $cm^3/(molecule*sec)$
Degradation : = 50 % after 1.9 hour(s)
Deg. product : No data
Method : other (calculated)
Year : 1981
GLP : No data
Test substance : No data

Remark : Concentration of substance: 10E-17 mole/l for OH radical
10 E-9 mole/l for phenol
half life: OH radical 100 hours for phenol
Peroxy radical 19.2 hours for phenol
Reliability : (2) valid with restrictions
14.09.2005 (31)

Type : water
Light source : No data
Light spectrum : No data
Relative intensity : No data
Deg. product : No data
Method : No data
Year : 1985

GLP	:	no data
Test substance	:	No data
Remark	:	By analogy with other Phenol compounds, resorcinol should degrade in water bodies by means of photochemically induced OH free radicals (concentration 10E-17 mol/l) and peroxy free radicals (concentration;10E-9 mol/l). For example; Half-life time for phenol approx 100 H (sensitizer OH) Half-life time for hydroquinone: 20 h (sensitizer OH)
Reliability 14.09.2005	:	(4) not assignable (89)
Remark	:	For undissociated resorcinol, a lamba max. of 274 nm and an epsilon max. of 2000 molE-1 x 1 x cmE-1, as well as a quantum yield of approx 0.03 at 253.3 nm were determined.
Reliability 02.06.2004	:	(4) not assignable (95)

3.1.2 STABILITY IN WATER

Type	:	No data
t1/2 pH4	:	No data
t1/2 pH7	:	No data
t1/2 pH9	:	No data
Deg. product	:	No data
Method	:	No data
Year	:	No data
GLP	:	no data
Test substance	:	no data
Remark	:	Resorcinol does not possess any functional groups that are regarded as being susceptible to hydrolysis, the soft ware prediction programme HYDROWIM v1.66 cannot estimate hydrolysis rate constants for phenols.
Reliability 14.09.2005	:	(2) valid with restrictions (129)

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

Type of measurement	:	background concentration
Media	:	food
Concentration	:	No data
Method	:	No data
Remark	:	Resorcinol was detected in roasted barley, in syrup and in coffee.
Result	:	Type of measurement: at contaminated site media: air result 8 µg per cigarette remark: resorcinol was quantitatively determined in cigarette smoke type of measurement: at contaminated site media: waste water result: 1 g/l remark: at USA Coal Liquification Plant type of measurement: at contaminated site media: waste water

result: 7-22 mg/l in ammonical liquid of coking process
150 mg/l in ammonical liquid of coking process
<0.1 mg/l in condensate from coking process
remark: USA coking operation.

14.09.2005 (20) (21) (44) (113) (115) (133)

Type of measurement : concentration at contaminated site
Media : other: waste water
Concentration : No data
Method : No data

Remark : An Indian author reports that resorcinol is a major waste water constituent in the manufacture of chemicals, fertilizers and dyes. No further information supplied.

14.09.2005 (63)

Type of measurement : concentration at contaminated site
Media : other:waste water
Concentration : No data
Method : No data

Remark : In the U.S.A., resorcinol was detected in concentrations of 7-22 mg/l in the ammonical liquid of two typical coking ovens. In a low-temperature coking oven, the resorcinol content of this liquid was 150 mg/l. In contrast, no resorcinol was detected in the condensate of one oven's waste gas or the waste water from a plant by a method with a limit of detection of 0.1 mg/l. (The original samples were each extracted with methyl isobutyl ketone, derivatized with trimethylsilyl ether and analysed by means of GC-FID.

14.09.2005 (21)

Type of measurement : concentration at contaminated site
Media : other: waste water
Concentration : No data
Method : No data

Remark : In the waste water from a coal liquefaction plant in the U.S.A., mg/l levels of resorcinol were determined by means of UV analysis

14.09.2005 (66)

(42)..□.□.□.□.□.□□□□□ **FIELD STUDIES**

(42)..□.□.□.□.□.□□□□□ **TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS**

Type : fugacity model level I
Media : other: air/water/soil/sediment
Air : 0 % (Fugacity Model Level I)
Water : 99.88 % (Fugacity Model Level I)
Soil : .06 % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other
Year : 2002

Method : Donald Mackay's Multimedia Environmental Models, The Fugacity Approach (1991)
Remark : Based on KOC of 2.94
Sediment: 0.07% (fugacity model level I)
Reliability : (2) valid with restrictions

07.06.2004 (61)

3.3.2 DISTRIBUTION

Media	:	air – biota – sediment(s) – soil – water
Method	:	Calculation according Mackay, Level I
Year	:	2002
Reliability	:	(2) valid with restrictions

19.05.2004 (62)

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	activated sludge, adapted
Concentration	:	related to COD (Chemical Oxygen Demand) related to
Contact time	:	No data
Degradation	:	97 (±) % after 4 day(s)
Result	:	Inherently biodegradable
Deg. Product	:	No data
Method	:	OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year	:	1990
GLP	:	No data
Test substance	:	No data
Method	:	The biodegradability of 161 mono- and disubstituted benzene-derivatives (including Resorcinol) was determined in the static test (Zahn-Wellens) and compared with the results of other laboratories. For Resorcinol, the result has been compared with that published by Tabak, H.H et al. Refer to reference 124 in this summary.
Result	:	Resorcinol is inherently biodegradable under the conditions of this test. Comparison of this data with that published by Tabak, H.H et al has confirmed this finding.
Reference	:	Wellens (1990): Z Wasser Abwasser Forsch 23, 85-89
Reliability	:	(2) valid with restrictions

14.09.2005 (135)

Type	:	aerobic
Inoculum	:	Other: see remark on method
Concentration	:	2300 mg/l related to Test substance
Contact time	:	120 hours
Degradation	:	95.3 (±) % after 3 day(s)
Result	:	Degradation
Deg. Product	:	Not identified
Method	:	Other: see remark
Year	:	1983
GLP	:	no data
Test substance	:	Other TS: see remark
Method	:	Organisms : Four organisms Pseudomonas, Penicillium, and two Candida strains were isolated in the laboratory by enrichment culture technique. All the four organisms in pure culture were used separately and jointly to study degradation of resorcinol in batch culture. Organisms able to grow in a

simple medium with minimum requirements for inorganics were isolated by enrichment technique using resorcinol (approximately 0.2 gm/100 ml) as the only carbon source.

Medium: The resorcinol basal medium (RBM) used for the isolation of microorganisms and the degradation of resorcinol contained per litre of tap water, KH_2PO_4 1.5 g, K_2HPO_4 1.5 g, $MgSO_4$ 0.3 g, NaCl 0.5 g, $(NH_4)_2SO_4$ 1.0 g and resorcinol 2.0 g.

Propagation: Liquid cultures were grown in 50 ml of sterile RBM at pH values 6, 7 and 8 in 250 ml conical flasks. Inocula were from the cultures previously grown in 10 ml RBM for 48 h. Incubation was carried out at room temperature (26-28°C) except for one set of experiment where the temperature effect was studied.
Effect of shaking on resorcinol degradation was studied by growing the cultures (as above) on rotary shaker operated at 30 rev. per minute.

Nitrogen source: The effect of ammonium hydrogen phosphate $[(NH_4)_2HPO_4)]$ cine potassium nitrate (KNO_3) was studied by replacing ammonium sulphate in RBM by these compounds. The nitrogen concentration was, however, maintained constant at 0.21 g N/l equivalent.
Mixed culture: The mixed culture of Pseudomonas + Penicillium + Yeasts and Pseudomonas + Penicillium were used to study their joint effect on degradation.

Estimation of Resorcinol: 5 ml medium was removed at regular intervals and was filtered through ordinary filter paper. The unutilized resorcinol in the medium was estimated by the method of Kolthoff and Belcher (1975).

Test substance : Resorcinol, no data on purity

Result : The degradation of resorcinol by indigenously isolated bacteria (Pseudomonas), mold (Penicillium) and yeast (Candida) was studied. Simple medium as tap water supplemented with phosphate and nitrogen was used for the degradation study. Mold and bacteria degraded 95.32% of resorcinol in 110 h in static culture and in 72 h in shake flask culture. However, 100% degradation was observed with mixed culture (mold + bacteria) in shake flask culture in 72 h. At 37°C bacteria degraded 90% resorcinol in static culture in 72 h.

The effect of nitrogen sources studies showed that $(NH_4)SO_4$ brought about the maximum degradation of resorcinol by mold and bacteria at pH 8.0 in comparison to $(NH_4)_2HPO_4$ and KNO_3. However, KNO_3 as a source of nitrogen brought about the degradation at a faster rate in case of bacteria and mixed culture (mold + bacteria).

Conclusion : Of the three types of organisms isolated (Candida, Penicillium and Pseudomonas), Candida cultures failed to give much degradation even at low pH values. Penicillium and Pseudomonas separately, as well as jointly, were capable of degrading resorcinol in acidic (pH 6), neutral (pH 7) and alkaline (pH 8) conditions. At pH 7 as well as pH 8, the degradation of 2300 mg/1 of resorcinol was noticed in about 120 h at room temperature. It was surprising to note that in addition to Pseudomonas, Penicillium could also degrade a higher concentration of resorcinol at pH 8.

Reference : Studies on the Biodegradation of Resorcinol by Indigenously Isolated Bacteria, Mold and Yeast
A.O. Ingle, H.J. Purohit and H.F. Daginawala, department of Biochemistry and Microbiology, Nagpur University, Nagpur-440 010, India

Reliability : (4) not assignable
No data on purity, no data on GLP, in-house method used

14.09.2005 (63)

Type : aerobic
Inoculum : Penicillium sp. (Fungi)

Concentration	:	2310 mg/l related to Test substance related to
Contact time	:	No data
Degradation	:	100 (±) % after 5 day(s)
Result	:	No data
Deg. Product	:	No data
Method	:	other
Year	:	No data
GLP	:	no data
Test substance	:	No data
Remark	:	measured degradation in aqueous medium at pH 7 and 8 using shaking culture/static culture.
Reliability	:	(4) not assignable

14.09.2005 (63)

Type	:	aerobic
Inoculum	:	other bacteria: activated sludge, phenol acclimated, mixed inoculum, including garden soil, compost
Contact time	:	10 days
Degradation	:	95% after 2 day(s)
Result	:	See remark
Deg. Product	:	Not identified
Method	:	other: see remark
Year	:	1964
GLP	:	no data
Test substance	:	Other TS: see remark

Method : Determination of degradation from oxygen consumption. In-house method for determination of microbial activity of selected phenol adopted bacteria.

Test conditions: The medium was prepared by aseptically adding concentrates to sterile distilled water. The final pH was 7-7.2. All cultures were incubated at room temperature on an orbital shaker. Subcultures in the same medium were made periodically for severall weeks or months. All traces of organic nutrients as debris carried in the original inoculum were rapidly lost, and all nonbacterial forms soon disappeared. As soon as the oxidative capacity of the selected bacteria could be demonstrated in media containing a low concentration of the phenolic substrate, 2 to 10 ml of this material were subcultured into media containing progressively increasing concentrations of the same compound. The increase in concentration of the substrate throughout the culture enrichment period ranged from 100 ppm to a maximum of 500 ppm.

Methods used in selecting or adapting organisms to degrade these compounds were soil perfusion, continuous feed activated sludge, primary enrichment in flasks on a shaker, and enrichment in batch-type fermentors.

Test substance : 104 aromatic compounds
Purity: highest purity grade reagents or practical grade reagents for laboratory syntheses.

Analytical method : Determination of the amount of phenolic substrate remaining:
At appropriate intervals during incubation, contents of flasks were restored to the original volume. For analysis of remaining phenolic compound, solids were separated by centrifugation; the supernatant fluid was filtered through a Whatman 50 filter paper. The 4-aminoantipyrine method (Ettinger, Ruchhoft, and Lishka, 1951; Mohler and Jacob, 1957) was used spectrophotometrically to determine residual concentrations of phenols other than nitrophenols. The color absorbance of aqueous solutions and chloroform extracts was determined at wavelengths of 460 and 510 mμ, respectively. The solutions of test compounds from the respective uninoculated control flasks were also analyzed to verify that any loss of substrate in the test flask was not due to volatilization loss or

chemical oxidation. To follow the increase in oxidative ability of organisms and make periodic determinations of the rate of dissimilation of phenols, the 4-aminoantipyrine test was modified for use as a semi-micro-method. This test required small amounts of medium and was useful as a rapid screen test for most of the non-nitrogenous compounds used.
Manometric studies. The purpose of the respirometric work was to determine whether organisms that had been adapted to utilize phenol could immediately degrade structurally related compounds to which they had not been adapted. The formation of adaptive enzymes to metabolize phenol was indicated by a marked lag in oxygen uptake in respirometric tests with phenol when organisms were grown in nutrient broth.
Phenol-adapted bacteria were inoculated in Gray and Thornton's liquid mineral salts medium containing 300 ppm of phenol as the only source of carbon, and incubated on a shaker at room temperature for 16 hr. The cells were then removed by centrifugation, washed several times with buffered dilution water, stored overnight at 5 C in the same buffer, aerated 3 to 4 hr, removed by centrifugation, and resuspended in 0.067 M phosphate buffer at pH 7.2. Each Warburg flask contained an appropriate amount of 0.067 M buffer at pH 7.2 and 0.5 ml of cell suspension in the main compartment, 0.2 ml of 10% KOH solution in the center well, and an amount of stock solution of substrate in the side arm necessary to produce the desired test concentration. The total volume of reagents and cell suspension added to a flask was 3.2 ml. A flask containing substrate without cell suspension was included for each compound to control chemical oxidation, along with an endogenous control and a test with phenol plus cells to confirm that the organisms used in the test had a normally high capacity to utilize phenol. The uniformity of oxygen uptake in the phenol controls indicated there was little variation in the activity of the cell suspensions used in different experiments. All flasks were incubated in a Warburg water bath at 30 C and shaken at a speed of 68 strokes per min. The gas phase was air. Results of 10-min observations of 0_2 uptake were averaged for each successive 30-min interval.
Chemical analysis of residual substrate. Whenever the observed oxygen uptake appeared to be significant, the centrifuged supernatant fluid from the respirometric test was analyzed for residual substrate. Phenols were analyzed by the same methods used during culture enrichment.

Result : 95 % degradation within 1-2 days for resorcinol. Breakdown products were not investigated.
Remarks: A considerable number of the enriched cultures were screened for adaptive enzyme formation. In all instances, an immediate and rapid oxygen uptake was observed in respirometric tests with the compound used in the original enrichment of the culture if the cells were harvested from a medium containing the same substrate as the sole source of carbon. A marked lag in oxygen consumption was noted in parallel tests when the bacteria were grown in nutrient broth.

Conclusion : The results of the study show that Dihydric phenols were generally oxidized; trihydric phenols were not. Cresols and dimethylphenols were oxidized; adding a chloro group increased resistance. Benzoic and hydroxybenzoic acids were oxidized; sulfonated, methoxylated, nitro, and chlorobenzoic acids were not; m-toluic acid was utilized but not the o- and p-isomers. Benzaldehyde and p-hydroxybenzaldehyde were oxidized. In general, nitro- and chloro-substituted compounds and the benzenes were difficult to oxidize.

Reference : Journal of Bacteriology Vol 87, No. 4 p. 910-919, Microbial Metabolism of Aromatic Compounds. Tabak et al. (1964): J. Bacteriol. 87, 910-919

Reliability : (4) not assignable

13.09.2005

(124)

Type : aerobic
Inoculum : other bacteria: activated sludge, perhaps acclimated
Concentration : 138 mg/l related to Test substance
related to
Contact time : No data
Degradation : 100 (±) % after 2 day(s)
Result : No data
Deg. Product : No data
Method : other: Modified German detergent tests
Year : No data
GLP : No data
Test substance : No data

Remark : Degradation related to DOC
Reliability : (4) not assignable
14.09.2005 (42)

Type : aerobic
Inoculum : activated sludge, non-adapted
Concentration : 100 mg/l related to Test substance
related to
Contact time : No data
Degradation : = 66.7 (±) % after 14 day(s)
Result : readily biodegradable
Deg. product : No data
Method : Other
Year : 1976
GLP : No data
Test substance : No data

Method : This study was conducted by the National Institute of Technology & Evaluation.

Activated sludge concentration: 30 ppm.
Analysis:
Total Organic Carbon was measured using UV-Vis at 100% and HPLC at 100% by direct measurement.
Reliability : (4) not assignable
14.09.2005 (90)

Type : aerobic
Inoculum : other: soil microflora from silt loam soil
Concentration : 25 mg/l related to Test substance
related to
Contact time : No data
Degradation : 100 (±) % after 8 day(s)
Result : No data
Deg. product : No data
Method : other: Test in closed bottles
Year : No data
GLP : No data
Test substance : no data

Remark : Test in closed bottles. Spectrophotometric determination at 275 nm
Test condition : Medium: aqueous mineral salts
Reliability : (4) not assignable
15.09.2005 (4)

Type : aerobic
Inoculum : activated sludge, adapted
Concentration : related to COD (Chemical Oxygen Demand)
related to

Contact time	:	No data
Degradation	:	90 (±) % after 15 day(s)
Result	:	No data
Kinetic of testsubst.	:	3 day(s) < 10 % 4 day(s) = 43 % 10 day(s) = 89 %
Deg. product	:	No data
Method	:	other: Zahn-Wellens Test in accordance with DIN 38412, Part 25
Year	:	1982
GLP	:	No data
Test substance	:	No data
Reliability	:	(4) not assignable

14.09.2005 (55)

Type	:	aerobic
Inoculum	:	activated sludge, adapted
Concentration	:	related to COD (Chemical Oxygen Demand) related to
Contact time	:	No data
Degradation	:	> 95 (±) % after 10 day(s)
Result	:	No data
Kinetic of testsubst.	:	5 = 87 %
Deg. product	:	No data
Method	:	other: Zahn-Wellens Test in accordance with DIN 38412, Part 25
Year	:	1980
GLP	:	No data
Test substance	:	No data
Reliability	:	(4) not assignable

14.09.2005 (55)

Type	:	aerobic
Inoculum	:	activated sludge, adapted
Concentration	:	related to COD (Chemical Oxygen Demand) related to
Contact time	:	No data
Degradation	:	> 95 (±) % after 7 day(s)
Result	:	No data
Kinetic of testsubst.	:	3 hour(s) = 2 % 1 day(s) = 28 % 3 day(s) = 75 %
Deg. product	:	No data
Method	:	other: Zahn-Wellens Test in accordance with DIN 38412, part 25 1975
Year	:	1975
GLP	:	No data
Test substance	:	No data
Reliability	:	(4) not assignable

14.09.2005 (55)

Type	:	aerobic
Inoculum	:	other bacteria: activated sludge, perhaps acclimated
Concentration	:	500 mg/l related to Test substance related to
Contact time	:	No data
Degradation	:	60 (±) % after 5 day(s)
Result	:	No data
Deg. product	:	No data
Method	:	other: modified German detergents test
Year	:	No data
GLP	:	No data

Test substance : No data

Remark : Degradation related to DOC
Reliability : (4) not assignable
14.09.2005 (42)

Type : aerobic
Inoculum : activated sludge, adapted
Concentration : 200 mg/l related to COD (Chemical Oxygen Demand)
related to
Contact time : No data
Degradation : 90 (±) % after 5 day(s)
Result : inherently biodegradable

Reliability : (4) not assignable
14.09.2005 (96)

Type : anaerobic
Inoculum : activated sludge, adapted
Concentration : 500 mg/l related to Test substance
related to
Contact time : No data
Degradation : 83 (±) % after 245 day(s)
Result : No data
Deg. product : No data
Method : other: Bottle Test, determination of gas production (CO2 and methane)
Year : No data
GLP : No data
Test substance : No data

Remark : sludge from waste water treatment plant
Reliability : (4) not assignable
14.09.2005 (7)

Type : anaerobic
Inoculum : activated sludge, adapted
Concentration : 1000 mg/l related to Test substance
related to
Contact time : No data
Degradation : 4 (±) % after 245 day(s)
Result : No data
Deg. product : No data
Method : other: Bottle test, determination of gas production (CO2 and methane)
Year : No data
GLP : no data
Test substance : no data

Reliability : (4) not assignable
14.09.2005 (7)

Type : anaerobic
Inoculum : activated sludge, adapted
Concentration : 500 mg/l related to Test substance
related to
Contact time : No data
Degradation : 30 (±) % after 196 day(s)
Result : No data
Deg. product : No data
Method : other: Bottle test, determination of gas production (CO2 and methane)
Year : No data
GLP : No data
Test substance : No data

Reliability : (4) not assignable
14.09.2005 (7)

Type : anaerobic
Inoculum : other: anaerobic sludge, acclimated
Concentration : 2000 mg/l related to Test substance
related to
Contact time : No data
Degradation : 0 (±) % after day(s)
Result : under test conditions no biodegradation observed
Deg. product : No data
Method : other: Bottle test, determination of gas production (CO2 and methane)
Year : No data
GLP : No data
Test substance : No data

Remark : No degradation after 245 days
Reliability : (4) not assignable
14.09.2005 (7)

Type : anaerobic
Inoculum : other bacteria: anaerobic sludge, municipal, acclimated
Concentration : 90 mg/l related to Test substance
related to
Contact time : No data
Degradation : 95 (±) % after 10 day(s)
Result : No data
Deg. product : No data
Method : other: submerged anaerobic upflow filter
Year : No data
GLP : No data
Test substance : No data

Remark : 95% of test substance degraded in hydraulic retention times of 2-10 days.
Test condition : Aclimation period: 110 hours
Reliability : (4) not assignable
14.09.2005 (19)

Type : anaerobic
Inoculum : other bacteria: Strain Re 10 (sulfate reducers)
Concentration : 220 mg/l related to Test substance
related to
Contact time : No data
Degradation : 100 (±) % after 4 day(s)
Result : No data
Deg. product : No data
Method : other:Turbidity test (measurement of absorbance at 500 nm)
Year : No data
GLP : no data
Test substance : no data

Remark : Turbidity test (measurement of absorbance at 500 nm).
Reliability : (4) not assignable
14.09.2005 (107)

Type : anaerobic
Inoculum : domestic sewage
Concentration : 10 related to Test substance
related to
Contact time : No data
Degradation : 0 (±) % after 56 day(s)

Result	:	No data
Deg. product	:	No data
Method	:	No data
Year	:	No data
GLP	:	no data
Test substance	:	no data
Remark	:	Waste water treatment plant in Jackson MI. Degree of degradation expressed in terms of methane production
Reliability	:	(4) not assignable

14.09.2005 (58)

Type	:	anaerobic
Inoculum	:	domestic sewage
Concentration	:	10 related to Test substance related to
Contact time	:	No data
Degradation	:	98 (±) % after 21 day(s)
Result	:	No data
Deg. product	:	No data
Method	:	No data
Year	:	No data
GLP	:	no data
Test substance	:	no data
Remark	:	Waste water treatment plant in Adrian MI. Degree of biodegradation expressed in terms of theoretical methane production
Reliability	:	(4) not assignable

14.09.2005 (58)

3.6 BOD5, COD OR BOD5/COD RATIO

BOD5

Method	:	other
Year	:	No data
Concentration	:	66.7 mg/l related to Test substance
BOD5	:	= 100 mg/l
GLP	:	No data

RATIO BOD5 / COD

BOD5/COD	:	ca. 1.74
Method	:	No data
Reliability	:	(4) not assignable

14.09.2005 (97)

3.7 BIOACCUMULATION

Elimination	:	No data
Method	:	other:calculated
Year	:	2004
GLP	:	No data
Test substance	:	Other TS
Method	:	EPIWIN v3.01 using BCFWIN v2.12
Result	:	Log BCF = 0.500 (BCF = 3.162)
Reliability	:	(2) valid with restrictions

14.09.2005 (128)

3.8 ADDITIONAL REMARKS

Remark : degration routes:
Through the agency of procaryotes and eucaryotes, resorcinol in aqueous medium can be metabolized via hydroxyhydroquinone (1,2,4-trihydroxybenzene) and maleyl acetate to beta-ketodipate and via hydroxyhydroquione and acetyl pyruvate to formic, acetic and pyruvic acids. In the presence of ozone, it can be degraded via pyrogallol (1,2,3-trihydroxybenzene) and 3-hydroxybenzoquione to glyoxalic acid, glyoxal, oxalic acid, CO2 and H2O

Reliability : (1) valid without restriction
26.05.2004

(16) (39) (76)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Leuciscus idus (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
NOEC	:	= 25
LC50	:	= 34.7
Limit test	:	no
Analytical monitoring	:	yes
Method	:	other: follows all major guidelines
Year	:	1981
GLP	:	no data
Test substance	:	other TS:
Remark	:	LC50 (96 hr): 95% confidence range: 34.7 - 46.8 mg/L. The study was carried out by Hoechst Aktiengesellschaft Pharmaceuticals Research Toxicology No data on GLP and stability of chemical solutions are provided. The study follows OECD, EU and OPPTS guidelines to a certain extent.
Test substance	:	Resorcin DS, Technical grade
Test condition	:	No data given for protocol deviations. Test fish: Golden ide (Leuciscus idus f. melantus) supplied by Paul Eggers, 2345 Hohenwestedt. Body weight: 1.5 - 2.7g Body length: 5.5 - 6.7cm Corpulence factor: 0.65 - 1.07 Test water: Deionised tap water Conductivity <5 µS/cm Added Salts - 192 mg NaHCO3, 120 mg CaSO4 . 2H2O, 120 mg MgSO4, 8 mg KCl. pH 8.0 - 8.3 Total hardness 9.5°d, carbonate hardness 6.4°d. Test facilities: The test tanks were made of glass and were filled with 20 liters of test water. The test temperature was held constant at 20 ±1°C by a water bath. The tanks were ventilated throughout the entire test period by means of glass capillary rods. Approximately 100 ml/min of air was fed through the tanks. The oxygen content was in excess of 7 mg/L. The tanks were lighted from above in a day-night rhythm of 12 hours each. The lighting intensity directly above the tanks was approximately 700 Lux. Conducting the test: Approximately 65 hours prior to the start of the test, 10 fish were added per test tank. The test substance, previously dissolved in test water, was applied to the test tanks and distributed evenly with a glass rod. Immediately prior to the addition of the test substance, as well as at 2, 24, 48, 72 and 96 hours, the parameters of pH, O_2 and temperature were measured in each test tank.
Result	:	Nominal concentrations: 0, 10, 25, 31.5, 40, 63 and 100 mg/L.

LC0 (96 hr) = 25 mg/L
LC50 (96 hr) = 34.7 mg/L
LC100 (96 hr) = 63 mg/L
NOEC (96 hr) = 25 mg/L
The results are based on nominal concentrations.

Calculated mortality of golden ide after exposure to resorcinol for 48 and 96 hr;

Conc (mg/L)	48hr % mortality	96 hr %mortality
0	0	0
10	0	0
25	0	0
31.5	10	20
40	60	90
63	100	100
100	100	100

Biological observations:
In the 31.5 to 100 mg/L groups 5 fish died up to 95 hours after addition of the test substance, with the following symptoms - surface swimming, uncoordinated swimming movements, drifting in a lateral position, hyperreflexivity, reduced frequency of gill action. The fish in the 25 and 10 mg/L groups did not differ in their behaviour from those in the control groups. The fish in the 100 mg/L group presented with punctate red flecks on the body surface. Dissection showed no macroscopically visible changes in all test groups.

The pH value and the measured oxygen concentration were in the same range as test values for the control groups.

Reference : Hoechst AG (1981): Acute Toxicity of Resorcin DS in Golden Ide (Leuciscus idus f. melanotus) (Report Number 200/81)

Reliability : (1) valid without restriction
14.09.2005

(53)

Type : flow through
Species : Pimephales promelas (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 Test #1 : = 29.5
LC50 Test #2 : = 26.8
Limit test : no
Analytical monitoring : yes
Method : other: see Remark
Year : 1981
GLP : no data
Test substance : other TS:

Test substance : Technical grade Resorcinol
Method : EPA-660/3/75-009, Methods of Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians (April, 1975); Standard Methods for the Examination of Water and Wastewater (14th Edition); Standard Method of Test for ASTM D1345-59 (Reapproved 1970) and published in the 1975 Annual Book of ASTM Standards - Part 31 - Water; or EPA Environmental Monitoring Series Publication, EPA-600/4-78-012 Methods for Measuring the Acute Toxicity of Effluents to Aquatic Organisms (January, 1978).
Result : Mean measured concentration:
Test #1 = 16.2, 25.8, 34, 39.6 and 46.4 mg/L
Test #2 = 12.8, 22.8, 32, 40 and 49.8 mg/L

Cumulative mortality %

Test #1

Conc (mg/L)	0	24	48	72	96 hr
0	0	0	0	0	0
16.2	0	0	20	20	20
25.8	0	0	10	30	40
34	0	40	40	80	90
39.6	0	70	70	80	80
46.4	0	80	80	90	100

Test #2

Conc(mg/L)	0	24	48	72	96 hr
0	0	0	0	0	10
12.8	0	0	0	10	10
22.8	0	0	0	30	60
32	0	10	60	60	60
40	0	60	80	80	80
49.8	0	40	70	90	90

Biological observations: no data available

Test condition : Environmental parameters remained within the limits throughout the study. Fathead minnows Pimephales promelas from Fender's Fish Hatchery, Route 1, Baltic, OH 43804. Test specimens were all the same year from 8 - 10 months old and 10 fish per test group were used.

Upon receiving the fish, treatment was carried out in the acclimation-holding tank combination. The fish container was placed in the acclimation tank containing dilution water where it was left to equilibrate to within ± 1°C with no more than 3°C change in any 12-hour period. Water from the acclimation tank was then poured into the receiving container and if no stress was indicated in 30 minutes, the fish were released from their shipping container to the acclimation tank. After 24 hours, pretreatment was started. The only variation made to the therapeutic treatment was the use of malachite green oxalate in one-half of the recommended concentration. This was used because Fender's Fish Hatchery cautioned that certain freshwater fish are sensitive to malachite green oxalate. After treatment was carried out, the tank was emptied and refilled with dilution water. The fish were held in this holding tank until used for testing. Water in the holding tank was aerated and circulated constantly by means of a 5 gpm pump with fiberglass filters attached. The water was also changed three times a week to remove any fish waste products that may not be removed by filtration.

Test water:
Dechlorinated water
pH 6.9 - 7.3 Test #1; 7.0 - 7.8 Test #2
Dissolved oxygen 8.0 - 9.6 Test #1; 8.3 - 10.6 Test #2
Temperature 18 - 21 °C Test #1; 10 - 22 °C Test #2
Conductivity 242 - 258 Test #1; 242 - 268 Test #2.

Test tanks: 10 gallon glass

The continuous flow-through system was equipped with one variable drive pump set to deliver dilution water at the rate of five volume changes in 24 hours in each test chamber, which was sufficient flow to maintain adequate concentrations of dissolved oxygen. The effluent pumps were sized and set to deliver concentrations needed to obtain an LC50. The diluter system was capable of maintaining the test concentration in each chamber within 5% of the starting concentration for the duration of the bioassay.

Reference : Fish Bioassay for resorcinol, report written by Koppers
Reliability : (1) valid without restriction

14.09.2005 (35)

Type	:	Semi-static
Species	:	Gambusia affinis (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50 24 hours	:	188.86 - 196.48
LC50 48 hours	:	185.7 - 188.3
LC50 72 hours	:	183.08 - 184.92
LC50 96 hours	:	179.56 - 182.47
Limit test	:	no
Analytical monitoring	:	yes
Method	:	other: see remark
Year	:	2000
GLP	:	no data
Test substance	:	Other TS:
Test substance	:	Analytical grade resorcinol and p-nitrophenol
Method	:	In house method, in principle follows OECD, EU and OPPTS guidelines. Healthy specimens of *Gambusia affinis*, collected from local freshwater ponds, were acclimated to laboratory conditions for 10 days in glass aquaria and fed daily with commercially prepared fish food. Feeding was discontinued one day prior to the commencement of the experiment and no feeding during the test period of 96 h. The fish selected were 2.5 - 3.4 cm in length and 0.25-0.4 g in weight. Test medium used was one day old tap water. Tests were conducted in triplicate, with a control. Ten fishes were exposed to each concentration of resorcinol from 180-190 mg/l. Stock solutions of the toxicants were prepared by using analytical grade reagent with deionised water. Dilution water: deionised water Test medium: dechlorinated tap water, 1 day old Temperature: 26-28°C pH 7.3-7.6 Dissolved Oxygen 6.9-7.2 mg/l total hardness: 70-80 mg/l CaCO3 Nominal concentrations of 180 and 190 mg/l. Test medium was renewed after every 24h. The dose mortality rate obtained was plotted and the LC50 values calculated. Also measured was the oxygen consumption rate which was expressed as mg of oxygen consumed/h/g of body weight.
Result	:	When fish were introduced into various concentrations of resorcinol (and p-nitrohenol) they showed abnormal swimming behavior for 24 hours at higher concentrations but at lower there was not much change in behaviour until 48 hours. After 48 hours, fish started showing erratic movements, loss of equilibrium surfacing and gulping of air. Blood clots in gills and mucus secretion for the fish exposed to resorcinol was observed. The 24, 48, 72 and 96 hr LC50 values for resorcinol for Gambusia affinis were 190.0, 187.0, 184.0 and 181.0 mg/l. Rate of oxygen uptake was significantly decreased at higher concentrations.
Reliability	:	(2) valid with restrictions In principle, the study follows the recognised guidelines, however, data on preparation on stock solutions stability, vehicle or exposure vessel type have not been included.
Reference	:	Acute Toxicity of Resorcinol and Nitrophenol to a Freshwater Fish, Gambusia Affinis and their Effects on Oxygen Uptake. Environment Science Laboratory, Department of Zoology, Karnatak University, Dharwad-580003, India

14.09.2005 (67)

Type	:	static
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50 (24 h)	:	= 88.6
LC50 (48 h)	:	= 72.6
LC50 (96 h)	:	= 53.4
Limit test	:	no
Analytical monitoring	:	yes
Method	:	other: Methods for Acute Toxicity with Fish, Macroinvertebrates and Amphibians EPA-600/3-75-009 (1975)
Year	:	1978
GLP	:	no data
Test substance	:	other TS:
Test substance	:	Resorcinol industrial grade
Method	:	GC/direct and photometric method used for analysis: phenol.

Statistical methods:
LC50's and confidence intervals were determined by either probit analysis (Finney, 1971; Barr et al., 1976), moving average method, or the binomial test (Stephan, 1977), depending on the number of partial kills observed. Each confidence interval describes the distribution of sensitivities of the test organisms; it does not indicate the precision of the acute mortality test.

Remark : Nominal concentration; oxygen saturation>/= 40%

Loading of fish per liter of dilution water was less than 0.8 g/L.

Result : Nominal concentration 56.5 mg/l
Measured concentration 49.5 mg/l

	LC50	Confidence interval
24 hr	88.6	72.3 - 113.6
48 hr	72.6	58.7 - 92.3
96 hr	53.4	41.1 – 72.1

The chemical was clearly toxic to freshwater organisms at concentrations below 500 mg/l.
Results based on nominal concentrations.

Test condition : No data given for protocol deviations.

Fathead minnows, Primephales promelas, from the EPA Newtown Fish Toxicology Station, Cincinnati, Ohio, were used for all freshwater tests. The fish ranged in size from 3.2 to 4.2 cm standard length, age is unknown. There were 5 fish per vessel with 2 vessels per concentration. They were held in circular fiberglass tanks with a 6 vol/day flow through of carbon-filtered tap water. The minnows were fed a twice daily ration of Tetra SM (Tetra-Werke, W. Germany) and were maintained on a 16 hr light to 8 hr dark diurnal cycle.
An initial prophylactic treatment for external parasites consisting of 5 mg/L potassium permanganate was ad-ministered on three consecutive days, then hygienic conditions were maintained by sterilizing all fish care equipment with a 200mg/L calcium hypochlorite (HTH) solution. The fish were observed for a minimum of 14 days (at least 10 days after any disease treatment) before being acclimated for testing.
The minnows were acclimated to the test dilution water quality and temperature over the first two days of a four-day acclimation period. Solution withdrawal and renewal twice daily accomplished the water quality transition and temperature was reduced from 25° to 22°C with the aid of a temperature bath-circulator. The fish were held for the last two days of acclimation at 22°C in 100% dilution water, and no food was given during the four-day period.
Reconstituted soft water of the following quality was used for all freshwater

tests: hardness, 40-48 mg/L as CaCO3 ; alkalinity, 30-35 mg/L as CaCO3 ; conductivity, 120-160 microhms/cm; and pH, 7.2-7.9. Test water was prepared in 378 L batches to ensure a consistent water quality for each test, and was intensely aerated prior to use. No further aeration was supplied during the 96 h test.

Bioassay procedures:
Five gallon distilled water bottles with the necks removed were used for bioassay aquaria. They were filled with 12 L of dilution water to a depth of approximately 24 cm. The day before a scheduled test, the aquaria were placed in temperature baths for cooling to 22° ± 1°C.
Toxicants were administered either directly or in the form of stock solutions in deionized water or acetone. The solutions were briefly stirred with a glass rod, then a water sample was withdrawn from one tank at each concentration for quantitative toxicant analysis. Five organisms were then placed in each of two duplicate aquaria for a total of 10 organisms tested per concentration. The loading of organisms per liter of dilution water was less than 0.8 g/L in all cases. The concentrations tested were arranged in geometric series with at least a 60% dilution factor. At least two control aquaria were run with additional control aquaria for any solvents used to introduce the toxicant into the test solutions. Control and solvent control mortality were less than 10% in all cases.
During the 96h test period, deaths were recorded and bodies removed when noticed. Percent survival, dissolved oxygen, and temperature were determined in each aquaria every 24 h. At the end of the test, pH was measured and another water sample was taken at each concentration, then control organisms were weighed and measured as an indication of the average size of organism used.

Reference : Acute Toxicity of 12 Industrial Chemicals to Fresh Water and Salt Water Organisms, Water Res. Vol 13, p137-141 (1979)

Reliability : (2) valid with restrictions
14.09.2005 (3)

Type : static
Species : Pimephales promelas (Fish, fresh water)
Exposure period : 48 hour(s)
Unit : mg/l
NOEC : = 72.6
Limit test : No data
Analytical monitoring : no
Method : other: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, EPA-600/3-75-009, 1975
Year : No data
GLP : no data
Test substance : no data

Remark : nominal concentration
Test condition : Saturation >=40%
14.09.2005 (24)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 24 hour(s)
Unit : mg/l
EC50 : 107.3
Analytical monitoring : no data
Method : other: QSAR
Year : 1987

GLP	:	no data
Test substance	:	Other TS:
Test substance	:	Purity > 95%
Method	:	AFNOR (1974): Determination of the mobility of Daphnia magna (90-301,12) Statistical method: Statistical analyses were conducted using STATITCF software in conjunction with an IBM PC AT computer. The structure-activity relationships between acute toxicity of 57 chemicals to Daphnia magna (24 h-IC50) and components of autocorrelation vectors of connectivity (C), Van der Waals volume (V), and electronegativity (E) have been examined. The equation log L/C = 14.718V0 - 3.375V3 + 0.3.49E2 - 0.220E4 - 3.902 was shown to be an excellent model for these compounds (r = 0.944). it has been used to predict ecotoxicological activity of many classes of compounds.
Result	:	The results were considered valid if dissolved oxygen measured at the end of the tests was at least equal to 25 % of saturation (2.27 mg/L of 02 at 20°C), if percentage of immobilization observed for the controls was zero, and if IC50 of the reference compound (potassium dichromate) ranged between 0.9 and 1.5 mg/L after 24 h exposure. Each chemical tested was assayed in duplicate for a minimum of 3 replicates on following days. 95% confidence range: 104.7-109.9 mg/l
Test condition	:	The 57 chemicals tested were purchased from different commercial sources and were not repurified before testing. They were diluted with AFNOR reconstituted hard water for toxicity tests (pH = 7.8 - 8.2 ; Hardness = 200 mg/l expressed as CaCO3). Acetone was used as dispersent-solvent for chemicals slightly soluble in water. The volume of acetone never exceeded 0.1 mL/L of reconstituted water. Due to high volatility of some of these compounds, tests were always carried out in closed systems. Species: The Daphnia magna Straus used in these experiments originated from the IRCHA Laboratory and has been cultured parthenogenetically in Pasteur Institute Laboratory since 1975. All were < 72 hrs old. The brood stock was kept in an environmental chamber at 22 ± 1°C, with a photoperiod of 16 hrs daylight/8 hrs darkness. Daphnids were fed with a diet of Chlorella vulgaris (1.0 X 10+6 cells/daphnid/hour). Methodology adopted for static tests with Daphnia manna (<72 hours old) was that published by AFNOR with slight modifications concerning the conditions in which they were raised. Daphnids were not fed during experimentations.
Conclusion	:	The QSAR study shows that a model using autocorrelation components can be used to predict the ecotoxicological activity of many classes of chemical compounds on Daphnia magna (alcohols, acids, aromatic compounds, pesticides). However, the results also show that the proposed model (Eq.4) cannot be applied to some pollutants such as small branched molecules or large linear molecules. Thus, the investigation reveals that it is very difficult to compute the "best" structure-toxicity-model for predicting ecotoxicological activities of all the compounds representing potential environmental hazard to living species. Under these conditions, and in agreement with other authors it is considered that further work is needed to reach this goal.
Reference	:	Devillers et al. (1987): Chemosphere 16, 1149-1163

Reliability	:	(2) valid with restrictions
14.09.2005		(27)
Type	:	flow through
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	µg/l
NOEC	:	172 measured/nominal
EC50	:	> 172 measured/nominal
LOEC	:	> 172 measured/nominal
MATC	:	> 172 measured/nominal
Limit Test	:	no
Analytical monitoring	:	yes
Method	:	other: See remarks
Year	:	2003
GLP	:	yes
Test substance	:	other TS: See remark
Test substance	:	Resorcinol USP Grade Flake, Lot 15-1 Purity 99.96%
Method	:	Conducted to: OECD Guideline No. 211 FIFRA Guideline 72-4 OPPTS Draft Guideline 850.1300
Test condition	:	21 day duration, 19 - 21 °C, illumination of 16 hours light: 8 hours darkness at 35 - 75 footcandles (380 - 810 lux) Dilution water: Fortified well water pH 8.0 - 8.2 Specific conductivity 500 microhms/cm Totat hardness as $CaCO_3$ 160 mg/L Total alkalinity as $CaCO_3$ 110 mg/L *Species*: At the initiation of the definitive study, Daphnia magna (≤ 24 hours old) were imparially selected and distributed to 24 unlabeled intermediate vessels (100 ml beakers) containing dilution water and several drops of algal food solution. The daphinids were impartially added, two at a time to each intermediate vessel, until each vessel contained two organisms. This process was repeated until each intermediate vessel contained ten organisms. The daphids were then introduced into the replicate exposure vessels by impartially selecting one of the unlabeled intermediate vessels containing ten organisms and gently pipetting them one at a time under the surface of the test solution. This process was repeated until the test concentrations and the controls contained forty Daphnia magna (10 organisms per replicate vessel) Food solutions were added to the exposure solutions prior to introduction of daphnids. *Test Monitoring*: The number of immobilized adult daphnids and observations of abnormal behavior were recorded daily. Immobilization is defined as the inability to swim within 15 seconds of gentle agitation of the test vessel. Survival of adult daphnids was determined daily during the exposure.
Reference	:	Lima (2004): Resorcinol - Full life Cycle Toxicity Test with Water Fleas, Daphnia magna Under Flow-through conditions. Lab ID Number: Springborn Smithers Study No. 13048.6404
Reliability	:	(1) valid without restrictions The information contained in this robust summary is obtained from a full life cycle toxicity test with water fleas (summarised in full in Section 4.5.2). Although this is not an acute toxicity study design test, observations were made of mortality and efffects on a daily basis including a measurement at 48 hours. From this a NOEC of 172 µg/l and an EC50 of >172 µg/l can be

obtained at 48 hours. This information is therefore considered to be useful for addressing the acute toxicity endpoint.

Therefore although the study itself is valid without restrictions, when it is used to support the acute toxicity to aquatic invertebrates endpoint it is considered to be reliable, but with restrictions.

14.09.2005 (77)

Type	:	static
Species	:	Multi-species study: Asellus intermedius (pillbug), Daphnia magna (water flea); Dugesia tigrina (flatworm), Gammarus fasciatus (sideswimmer), Helisoma trivolvis (snail), Lumbricus variegatus (segmented worm) and Pimephales promelas (fathead minnow)
Exposure period	:	96 hour(s)
Unit	:	mg/l
EC50	:	No data
Analytical monitoring	:	no
Method	:	other: multi-species method, not conducted to guidelines
Year	:	1985
GLP	:	No data
Test substance	:	Other TS:

Test substance	:	Resorcinol reagent grade
Method	:	Method followed was an expansion of established procedures using the following methodologies: U.S. Environmental Protection Agency, 1975. Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians. Committee on Methods for Toxicity Tests with Aquatic Organisms. Ecology Series. EPA-600/3-75-009. Duluth, MN. American Public Health Association, American Water Works Association and Water Pollution Control Federation. 1985. Standard Methods for the Examination of Water and Wastewater, 16th ed. American Public Health Association, Washington, DC, pp. 689-823. American Society for Testing and Materials. 1980. Standard practice for conducting acute toxicity tests with fishes, macroinvertebrates, and amphibians. ASTM Standard E 729-80. Philadelphia, PA, pp. 1-25. The static multispecies bioassays were performed in seamless glass, 30.5-cm cuboidal, Pyrex chromatography jars to which 20 liters of test solution was added. Water quality was routinely monitored to characterize the diluent water and ensure its suitability. Activated carbon-filtered, de-chlorinated and tempered industrial service water from Lake Ontario was used in all tests. The minnows and snails were placed in the test vessels. The remaining five species were segregated in welded stainless steel, 55-mesh wirecloth baskets (5.5 cm in diameter x 7.5 cm in depth). Each basket was suspended from a 1-rpm motor-driven mechanism that raised and lowered the baskets in the water column. A stainless steel band, slotted every 0.5 cm, facilitated the position of the baskets so that the submerged volumes changed from one-third to two-thirds during each cycle. The baskets were spaced around the test vessel rim so that they did not interfere with each other. One-half of the volume of the submerged basket was exchanged with the main tank volume every minute. Age at study initiation: Asellus intermedius (pillbug): Juveniles as uniform in size as possible (approximate size 0.012 g) Daphnia magna (water flea): Juveniles as uniform in size as possible (first and second larval instar) Dugesia tigrina (flatworm): Juveniles as uniform in size as possible (approximate size 0.006 g) Gammarus fasciatus (sideswimmer): Juveniles as uniform in size as

possible (approximate size 0.007 g)
Helisoma trivolvis (snail): Juveniles as uniform in size as possible (approximate size 0.180 g)
Lumbricus variegatus (segmented worm): Juveniles as uniform in size as possible (approximate size 0.006 g)
Pimephales promelas (fathead minnow): Juveniles as uniform in size as possible (0.2-0.5 g)

Test solutions
The chemicals used in the tests were reagent-grade. Resorcinol is readily soluble and so was added directly to the diluent water in each aquarium in the appropriate amounts to give nominal concentrations of 100, 10, 1 and 0.1 mg/L. Test chemical concentrations were not analyzed. Once the test solutions were prepared, the starting temperature, dissolved oxygen and pH values were determined for each exposure concentration and the control. When the starting pH of the test solution fell outside the extremes of 6.5 to 8.5, the pH was adjusted to 7.0 by the addition of 10% (v/v) NaOH or 10% (v/v) H_2SO_4.

Physical/chemical parameters
Determinations of the temperature, dissolved oxygen and pH of each test solution were made in conjunction with the daily biological observations. The test temperature target was 20 ± 1°C. If the dissolved oxygen concentration in a test chamber fell below 40% of the starting level in a test, the test was repeated with 0.05 L/min glass-sparger aeration. All tests were conducted within the extremes of 6.5 to 8.5 pH units. The photoperiod duration was 16 h of light. The air-water interface of each tank received approximately 50 ft-c of cool-white fluorescent light.
Total dissolved solids: 180 mg/l
Total hardness ($CaCO_3$) 130 mg/l
Noncarbonate hardness (as $CaCO_3$)
Alkalinity (as $CaCO_3$): 93 mg/l

Biological parameters
Biological observations were made daily. Survival, condition and behavorial information were recorded. Dead organisms were removed when observed. A test organism was considered dead if it appeared motionless and exhibited no response to gentle prodding. If more than one-half of the population of a species exposed in any treatment was determined to be dead, additional aquaria containing lower concentrations of test solution were set up. All seven species were exposed to each dose level. At any time during the test when all 10 organisms of a species were considered dead, these biological parameters were determined and recorded. All species in these tests were exposed for the same time period, 96 h. As in any bioassay that determines a dose response, the LC50 value can be achieved at any time during the exposure.
Statistics: The LC50 values were estimated by an interpolation method using a computer program written for aquatic toxicity. This linear interpolation uses the logarithm transformation of the concentration and the angle of transformation of the percent dead between the two doses that bracket 50% response (i.e. proportion killed). The moving average and prohibit methods could not be used because the required minimum of two partial mortalities was rarely obtained.
Remarks: there may be an increased sensitivity in this test due to the greater duration of a 96-hours.

Results : LC50:

Asellus intermedius (pillbug): > 100 mg/l

Daphnia magna (water flea): 0.25 mg/l

Dugesia tigrina (flatworm): > 100 mg/l

Gammarus fasciatus (sideswimmer): > 100 mg/l

Helisoma trivolvis (snail): > 100 mg/l

Lumbricus variegatus (segmented worm): > 100 mg/l

Pimephales promelas (fathead minnow): 40 mg/l

Reference : Ewell et al. (1986): Environ. Toxicol. Chem. 5, 831-840
Reliability : (2) valid with restrictions
14.09.2005 (32)

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : <= .8
Analytical monitoring : no data
Method : other: not performed to any guidelines
Year : No data
GLP : no data
Test substance : no data

Remark : EC50 pronounced harmful effect on 50% or more of Daphnia
Test condition : At the end of the study, the creatures were treated with electro-acoustic waves and the number of harmed creatures that lay immobile on the bottom were determined.
Beta-mesosaprobic and mesotropic river water was used for dilution.
Reliability : (4) not assignable
15.09.2005 (13)

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : 1.28
Analytical monitoring : no data
Method : other: study not conducted to any guideline
Year : No data
GLP : no data
Test substance : no data

Remark : 95% Confidence range 0.50-1.62 mg/l
Reliability : (4) not assignable
14.09.2005 (47)

Type : No data
Species : Palaemonetes pugio (Crustacea)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 (24h) : = 169.5
LC50 (48 h) : = 78
LC50 (96h) : = 42.2
Analytical monitoring : yes
Method : other: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, EPA-660/3-75-009, 1975
Year : 1978
GLP : No data
Test substance : Other TS:

Test substance : Resorcinol industrial grade
Method : GC/direct and photometric method used for analyses: phenol

Statistical methods:

LC50s and confidence intervals were determined by either probit analysis (Finney, 1971; Barr et al., 1976), moving average method, or the binomial test (Stephan, 1977), depending on the number of partial kills observed. Each confidence interval describes the distribution of sensitivities of the test organisms: it does not indicate the precision of the acute mortality test.

Remark : Artificial brackish water (pH: 8.3 - 8.7; salinity: 25+/- g/l) was used for dilution.
LC50 24 h confidence intervals: 136.7-230.7 mg/l
LC50 48 h 95% confidence intervals: 61-106.5 mg/l
LC50 96 h 95% confidence intervals: 30.9-60.6 mg/l.

Test Condition : Grass shrimp, Palaemonetes pugio, collected from an estuary in Galveston Bay system were used for most saltwater testing. All shrimp were maintained in static solutions of 25 ppt Instant Ocean (Aquarium Systems, Inc Eastlake Ohio) filtered with air lift basket filters containing carbon and oyster shell. They were fed a cereal-type pellet supplied by Texas A&M and were maintained on a 16 hr light – 8 h dark diurnal cycle. Only minimal acclimation procedures were necessary since the shrimp were held for a minimum of 10 days under testing conditions (25 ppt salinity, 21-23°C) Temperature in holding tanks was monitored for 48 hr period to detect any gross fluctuations from 22°C. The organisms were not fed during this 48 hr period to prevent fouling in the test aquaria. Instant Ocean synthetic seawater was used as the test dilution water. Salinity (25 +/- 1 ppt), conductivity, and pH (8.3-8.7) were measured on each 378 L batch and the water was intensely aerated prior to use.

Bioassay procedures:
Five gallon distilled water bottles with the necks removed were used for bioassay aquaria. They were filled with 12 L of dilution water to a depth of approximately 24 cm. The day before a scheduled test, the aquaria were placed in temperature baths for cooling to 22° ± 1°C.
Toxicants were administered either directly or in the form of stock solutions in deionized water or acetone. The solutions were briefly stirred with a glass rod, then a water sample was withdrawn from one tank at each concentration for quantitative toxicant analysis. Five organisms were then placed in each of two duplicate aquaria for a total of 10 organisms tested per concentration. The loading of organisms per liter of dilution water was less than 0.8 g/L in all cases. The concentrations tested were arranged in geometric series with at least a 60% dilution factor. At least two control aquaria were run with additional control aquaria for any solvents used to introduce the toxicant into the test solutions. Control and solvent control mortality were less than 10% in all cases.
During the 96h test period, deaths were recorded and bodies removed when noticed. Percent survival, dissolved oxygen, and temperature were determined in each aquaria every 24 h. At the end of the test, pH was measured and another water sample was taken at each concentration, then control organisms were weighed and measured as an indication of the average size of organism used.

Reference : Acute Toxicity of 12 Industrial Chemicals to Fresh Water and Salt Water Organisms, Water Res. Vol 13, p137-141 (1979)

Reliability : (2) valid with restrictions
14.09.2005

(3)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : other algae: other aquatic plant: see remarks
Endpoint : other: toxicity to algae
Exposure period : No data
Unit : No data
Method : other: In-house method see remarks

Year	:	1981
GLP	:	no data
Test substance	:	other TS: see remark
Test substance	:	14 different phenolic compounds no data Purity: No data
Method	:	In-house method for determination of toxicity to algae and aquatic spermatophytes. Element basis: % inhibition on chlorophyll fluorescence, motility of algal flagellates and cytoplasmic streaming of aquatic spermatophytes. Analytical method: yes Statistical method: no
Remark	:	Species/strain/supplier: Cyclotella cryptica (WERNER 1969), Dunaliella salina (MILKO 1962), Chlamydomonas reinhardii strain 137, (WERNER & PAWLITZ 1978), Lemna minor (WERNER 1967) and Euglena gracilis (MARCENKO 1972). Nitella sp. from Lake Baikal was grown as described in (STOM et al. 1974). Elodea canadensis was collected in the Angara river and kept for adaptation at least one week. Vallisneria spiralis was received from the museum collection of the Faculty of Biology, State University (Irkutsk) and cultivated according to STOM (1977). E. canadensis was cultivated at 16°C and L. minor at 24°C in petri dishes (20 cm diameter), both at 800 lux and a light dark regime of 9:15 h. Exposure period: 5 and 15 minutes, 9 and 12 days.
Result	:	Nominal concentrations: 0.01 and 0.0001 M Unit: % inhibition NOEC: Not determined. The mechanism of the inhibition of the phenolic compounds is a sensitive reaction. The lowest effective concentration found (with 100% efficiency) is about 6 E-07 M with a-naphthoquinone. By classical chemical methods these concentrations are very difficult to determine Control: yes The following observations were seen within 15 minutes of exposure to resorcinol: -30% and 10% decrease in intensity of chlorophyll fluorescence was observed in C. cryptica with 0.01M and 0.0001M resorcinol, respectively. - The control gave satisfactory response. At 0.001M concentration, fluorescence was reduced to 6.5% of the control. - Total inhibition of motility of D. salina and Nittela sp. was observed with 0.05M resorcinol. - Total inhibition of motility of C. reinhardii and e. gracilis was observed with 0.025M and 0.04M resorcinol, respectively. Cytoplasmatic streaming of V. spiralis was observed with 0.5M and 0.05M resorcinol for leaves and roots, respectively. The following observations were seen within 9 and 12 days of exposure to resorcinol: - 50% inhibition of plant multiplication in L. minor within 12 days and growth of E. canadensis within 9 days was observed with 0.0015M and 0.0013M resorcinol, respectively.

Test condition	:	In the experiments with Nitella sp., E. canadensis, L. minor and V. spiralis, phenols were dissolved in tap water; with algae the phenols (including resorcinol) were dissolved in the media used for cultivation. In the experiments with E. canadensis and L. minor the media were exchanged after 24 h. Effects on cytoplasmic streaming in E. canadensis and V. spiralis were analyzed according to STRUGGER (1949) and STOM & KOZHOVA (1976), in Nitella sp. according to STOM et al. (1974). Methods for calculating concentrations: Chlorophyll fluorescence was recorded with a microspectrofluorometer. It was constructed on the basis of a "FLUO VAL" fluorescent microscope and a "SPECOL" monochromator (Carl ZEISS, Jena, GDR). The instrument had a photo-electronic multiplier (FEU-79 and a micro-voltmeter V-623. Fluorescence of the internodes of Nitella sp. was registered at 685 nm, the maximum of chlorophyll fluorescence. Chlorophyll fluorescence in Cyclotella cryptica was studied in a haemocytometer (Gorjaev chamber) with successive measurements at different positions in the algal cell. Phenols were estimated by gas chromatography and polarography (SUSLOV & STOM 1978). Total amount of quinoid products of phenol oxidation was determined potentiometrically (STOM et al. 1972).
Conclusion	:	Based upon the results of this study, it was concluded that the toxicity of meta-isomers and methylated phenols is lower than that of ortho and para-diphenols. Comparing ortho and par-isomers of the same substance the results are not uniform. There are organisms, for which para-isomers are more toxic (Cyclotella cryptica, Dunaliella salina, Chlamydomonas reinhardii, Vallisneria spiralis), and others, for which ortho-isomers are more toxic (Nitella sp., Euglena gracilis, Elodea cana-densis). This suggests that most compounds tested affect unspecifically cell proteins, structural proteins in cell organelles as well as cytoplasmic proteins involved in cell motility and cytoplasmic streaming. However, since we do not understand well the mechanisms of the two processes mentioned, the effects of these unspecific inhibitors are difficult to explain. Cytoplasmic streaming and cell motility are energy consuming processes. Unspecific inhibition of the ATP generating system in the cells therefore certainly will affect these processes (NULTSCH 1974). On the other hand, also an unspecific blocking of SH-groups (e.g., by PCMB) will stop movement of cell organelles such as chloroplasts (SCHONBOHM 1972).
Reference	:	Stom, Roth (1981): Bull. Environ. Contam. Toxicol. 27, 332-337
Reliability	:	(4) not assignable Klimisch code (4); not asignable due to unspecific effects of phenolic compounds seen at various endpoints that were investigated, which mechanisms is still not known and could not be explained.

14.09.2005 (123)

Species	:	Chlorella pyrenoidosa (Algae)
Endpoint	:	growth rate
Exposure period	:	2, 4, 6, 24 and 48 hours
Unit	:	mg/l
EC0	:	1.1
Limit test	:	No
Analytical monitoring	:	No
Method	:	other: Determination of Cell Division Rate; investigation not performed to guideline "Cellmultiplication-inhibition Test"
Year	:	1987
GLP	:	no data
Test substance	:	no data

Test condition	:	Chlorella pyrenoidosa was maintained in MBL medium (Stein 1973) at normal and 1/100 the normal iron (i.e. 6.5 µg Fe l^{-1}) and trace metal

concentrations. All cultures were maintained on a 12 hour light: 12 hour dark cycle (Philips TL 40 W fluorescent white, 6400 lux) at 21°C. Cells in log-phase growth were used for all experiments.

Method : Chlorella pyrenoidosa assays used 50 ml standard softwater (NaHCO 48 mg/l, $CaSO_4.2H_2O$ 30 mg/l, $MgSO_4$ 30 mg/l KCl 2 mg/l) with the addition of 1 ml of 0.5 M Hepes buffer (pH 7.0), 0.5 ml $NaNO_3$ (2.1 g/l) and 0.5 ml of K_2HPO_4 (0.22 g/l). Cell density was measured initially and on three subsequent days by counting in a haemocytometer. A regression line was fitted to a plot of log (cell density/initial cell density) vs time, and cell division rate (u) was determined from the slope or expressed as cell divisions/ day (3.32 u)
Resorcinol was tested at a nominal concentration of 10^{-5} M.

Results : Cell division rate, expressed as a percentage of the blank was 103%. The blank cell division rate was 0.1349 +/- 0.017 (mean of duplicates).

Conclusion : No reduction in cell division rate in Chlorella pyrenoidosa was observed with a resorcinol concentration of 10^{-5} M.

Remark : Static test only one concentration tested. Toxicity of test substance measured along side that of copper complexes to demonstrate effects of copper on growth rate.

Reference : Mechanisms of toxicity of ionic copper and copper complexes of algae J.L. Stauber and T.M. Florence, CSIRO, Division of Energy Chemistry, Lucas Heights Research Laboratories, Private Mail Bag 7, Sutherland, New South Wales 2232, Australia

Reliability : (2) valid with restrictions
14.09.2005 (118)

Species : Chlorella vulgaris (Algae)
Endpoint : biomass
Exposure period : 6 hour(s)
Unit : mg/l
EC50 : 835
Method : other: growth inhibition test
Year : No data
GLP : no data
Test substance : no data

Remark : Absorbance measurement at 680nm; temperature: 36.5°C
Absorbance measurement at 750nm; temperature: 36.5°C
Concentration was determined which caused 50% inhibition of autotrophic growth of synchronous Clorella vulgaris suspensions.

Reliability : (4) not assignable
14.09.2005 (72)

Species : Dunaliella salina (Algae)
Endpoint : other: Inhibition of spontaneous movement
Exposure period : 15 minute(s)
Unit : mg/l
EC100 : = 4404
Method : other: Determination of the lowest concentration that causes inhibition of spontaneous movement after 15 minutes for the single cell algae
Year : No data
GLP : no data
Test substance : no data

Reliability : (4) not assignable
12.09.2005 (122)

Species : Dunaliella salina (Algae)
Endpoint : other: inhibition of spontaneous movement
Exposure period : 3 hour(s)
Unit : mg/l
EC100 : 1652

Method	:	other: Determination of the lowest concentration that causes inhibition of spontaneous movement after 15 minutes for the single cell algae
Year	:	No data
GLP	:	no data
Test substance	:	no data
Reliability	:	(4) not assignable

12.09.2005 (122)

Species	:	Nitella sp. (Algae)
Endpoint	:	other: Inhibition of Plasma flow
Exposure period	:	15 minute(s)
Unit	:	mg/l
EC100	:	= 5506
EC100 (3 h)	:	= 2202
Method	:	other: Determination of the lowest concentration that causes inhibition of plasma flow after 15 minutes
Year	:	No data
GLP	:	no data
Test substance	:	no data
Remark	:	Test condition: 10-15°C
Reliability	:	(4) not assignable

12.09.2005 (122)

Species	:	other aquatic plant: Elodea canadensis (Canadian pondweed)
Endpoint	:	other: Chloroplast movement
Exposure period	:	15 minute(s)
Unit	:	mg/l
EC100	:	= 1101
Method	:	other: Observation of chloroplast movement
Year	:	No data
GLP	:	no data
Test substance	:	no data
Reliability	:	(4) not assignable

12.09.2005 (122)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type	:	No data
Species	:	Aspergillus sp. (Fungi)
Exposure period	:	6 day(s)
Unit	:	mg/l
EC100	:	2000
Method	:	other: Growth inhibition test
Year	:	No data
GLP	:	no data
Test substance	:	no data
Remark	:	Acetone used as solubilizer; concentrations of 500, 700, 1000 and 2000 mg/1 caused 45, 60, 95 and 100% inhibition of mycelium growth.
Reliability	:	(4) not assignable

14.09.2005 (30)

Type	:	No data
Species	:	other fungi: Aspergillus fumigatus
Exposure period	:	5 hour(s)
Unit	:	mg/l
Method	:	other: Growth inhibition test

Year	:	No data
GLP	:	no data
Test substance	:	no data
Remark	:	Exposure of spores (duration of exposure 4.5h = 50% germination of control) to 1 g resorcinol/1 liquified agar had no significant effect on the spore germination rate. However, at a concentration of >=500 mg/1, shortening of the germ tubes was observed.
Reliability	:	(4) not assignable

14.09.2005 (64)

Type	:	No data
Species	:	other fungi: Penicillium chrysogenum
Exposure period	:	5 day(s)
Unit	:	mg/l
Method	:	other: Growth inhibition test
Year	:	No data
GLP	:	No data
Test substance	:	No data
Reliability	:	(4) not assignable

14.09.2005 (48)

Type	:	No data
Species	:	Saccharomyces cerevisiae (Fungi)
Exposure period	:	48 hour(s)
Unit	:	mg/l
Ec100	:	> 6400
Method	:	other: Growth inhibition test
Year	:	No data
GLP	:	no data
Test substance	:	no data
Reliability	:	(4) not assignable

14.09.2005 (48)

Type	:	aquatic
Species	:	Escherichia coli (Bacteria)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC80	:	<= 40000
Method	:	other: Growth inhibition test (test parameter: colony formation)
Year	:	No data
GLP	:	no data
Test substance	:	no data
Remark	:	The lowest concentration that caused 70% growth inhibition.
Reliability	:	(4) not assignable

14.09.2005 (34)

Type	:	aquatic
Species	:	Escherichia coli (Bacteria)
Exposure period	:	16 hour(s)
Unit	:	mg/l
EC70 (48h)	:	<= 40000
Method	:	other: Inhibition of glucose degradation: investigation not performed to any guideline.
Year	:	No data
GLP	:	no data
Test substance	:	no data
Remark	:	SG = harmfulness threshold

The effect of toxins on the metabolic process manifests itself in a slower drop in pH in the damaged cultures than in the control cultures.
Temperature @ 25°C; initial pH: 7.5-7.8; dilution water: Water from the receiving stream filtered until no longer turbid.

Reliability : (4) not assignable
14.09.2005 (14)

Type : aquatic
Species : Pseudomonas fluorescens (Bacteria)
Exposure period : 16 hour(s)
Unit : mg/l
EC70 (48h) : <= 40000
Method : other: Inhibition of glucose degradation; investigation not performed to any guideline
Year : No data
GLP : no data
Test substance : no data

Remark : SG: harmfulness threshold
The effect of toxins on the metobolic process manifests itself in a slower drop in pH in the damaged cultures than in the control culture.
Test condition: temperature @ 25°C; initial pH @ 7.5-7.8; Dilution water: water from the receiving stream filtered until no longer turbid.
Reliability : (4) not assignable
14.09.2005 (14)

Type : aquatic
Species : other fungi: Chaetomium cupreum
Exposure period : No data
Unit : No data
Method : other: Growth inhibition test
Year : No data
GLP : no data
Test substance : no data

Remark : The soil fungus grows in aqueous medium containing resorcinol as the sole source of carbon.
Reliability : (4) not assignable
14.09.2005 (8)

Type : aquatic
Species : other fungi: Drechslera oryzae
Exposure period : No data
Unit : mg/l
Method : other: Growth inhibition test
Year : No data
GLP : No data
Test substance : No data

Remark : The parasitic fungus grows in aqueous medium containing resorcinol as the sole source of carbon; growth inhibition occurs from >=2202 mg/l.
Reliability : (4) not assignable
14.09.2005 (8)

Type : aquatic
Species : other fungi: Fusarium oxysporum
Exposure period : No data
Unit : No data
Method : other: Growth inhibition test (test parameter: colony formation)
Year : No data
GLP : no data
Test substance : no data

Remark	:	The parasitic fungus grows in aqueous medium containing resorcinol as the sole source of carbon; growth inhibition occurs from >=2202 mg/l
Reliability	:	(4) not assignable
14.09.2005		(8)
Type	:	other: Agar plate
Species	:	Fusarium sp. (Fungi)
Exposure period	:	14 hour(s)
Unit	:	No data
Method	:	other
Year	:	No data
GLP	:	no data
Test substance	:	no data
Remark	:	Exposure of spores (duration of exposure 13.5 h = 50% germination of the control) to 1 g resorcinol/1 liquified agar had no significant effect on the spore germination rate.
Reliability	:	(4) not assignable
14.09.2005		(64)
Type	:	other: Agar plate
Species	:	other bacteria: Xanthomonas campestris pv. betlicola
Exposure period	:	48 hour(s)
Unit	:	mg/l
Method	:	other: Spot test
Year	:	No data
GLP	:	no data
Test substance	:	no data
Remark	:	50-250 mg/1; 3 plates/concentration; concentration-dependent growth inhibition (inhibition zone: max 35 mm); plant-pathogenic bacterium; in vivo: monthly spraying with 250 and 500 ppm for 7 months effected 68.35 and 72.15% disease control.
Reliability	:	(4) not assignable
14.09.2005		(127)
Type	:	other: Colony diameter on agar plate
Species	:	other fungi: Fusarium oxysporum (soil fungus)
Exposure period	:	6 day(s)
Unit	:	mg/l
EC50	:	ca. 1101
Method	:	other: Growth inhibition test
Year	:	No data
GLP	:	No data
Test substance	:	No data
Remark	:	Test condition @ 25°C
Reliability	:	(4) not assignable
14.09.2005		(116)
Type	:	No data
Species	:	Candida utilis (Fungi)
Exposure period	:	48 hour(s)
Unit	:	No data
EC100	:	> 6400
Method	:	other: Growth inhibition test
Year	:	No data
GLP	:	no data
Test substance	:	no data
Reliability	:	(4) not assignable

14.09.2005 (48)

4.5.1 CHRONIC TOXICITY TO FISH

Species	:	Brachydanio rerio (Fish, fresh water)
Endpoint	:	other:malformations and embryolethality
Exposure period	:	7 day(s)
Unit	:	mg/l
EC50	:	= 54.8
LC50	:	= 262
Analytical monitoring	:	no data
Method	:	OECD Guide-line draft "Early Life Stage Test (ELS-Test)"
Year	:	1989
GLP	:	no data
Test substance	:	Other TS:
Test substance	:	Resorcinol ≥99%
Method	:	Statistical Methods: Unfertilized eggs were excluded from the calculations and corrections were made for mortality in the controls in the statistical analyses. LC50 and 95% confidence intervals were calculated according to Litchfield and Wilcoxon (1949) or Kooyman (1981). If a test yielded concentrations without partial kills, the geometric mean of the 0 and 100% effect concentrations was taken as the LC50 and binomial confidence limits were calculated (Stephan, 1977). The same procedure was applied to the calculation of the EC50, after frequencies of embryonic mortality and abnormal development observed in the posthatch larvae were combined. Differences in mean survival and abnormal development under the experimental concentrations were tested against the blank control by means of a x^2 test (Sokal and Rohlf, 1981). Concentrations affecting survival by more than 50% were excluded from the statistical analyses as size-selective mortality might occur. Data on embryotoxicity of the species were compared by means of orthogonal regression analysis.
Test condition	:	Fertilized eggs of zebra fish in the blastula stage (2 to 4 hr after spawning) were obtained from an in-house laboratory culture. Eggs were disinfected for 1 min in a 0.04% formalin solution before transferring them into 60-ml glass test vessels filled with 50 ml test solution. The test medium used was aerated reconstituted water, prepared according to Alabaster and Abram (1965) with a pH of 8.4 ± 0.2 and a hardness of 250 mg/liter (as CaC03). The embryolarval stages were exposed continuously for 7 days to five to seven toxicant concentrations and a control. Tests with zebra fish were not duplicated. The range between the concentrations was 3.2. Sixty eggs were exposed per concentration. The test solutions were renewed three times a week, leaving the eggs or larvae in the test vessels while the water was changed. No food was provided for the larvae. In order to minimize compound decomposition, the stock solutions were prepared fresh at each renewal. Mean pH and oxygen concentrations were 8.4 ± 0.2 and 8.1 ± 0.2. The actual concentrations of the test compounds were not verified during the experiments. The toxicity tests were performed in a constant-temperature room at 25 ± 1°C and a photoperiod of 12 hr. Dead prehatch and posthatch larvae were counted and removed daily. At the end of the test, surviving fish were anesthetized in buffered tricaine methane sulfonate (MS 222, Sandoz, Basel) and the number of macroscopically malformed fish was determined under a binocular (amplification 30X).
Remark	:	The zebra fish test formed part of a larger study comparing the ELS toxicity of zebra fish (7 days) and rainbow trout (60 days) with a view to using the zebra fish test as a short-cut method both for environmental hazard assessment and for screening of direct-acting human teratogens.

Result	:	EC50 (weight): 54.8 mg/l LC50 (embrolethality): 262 mg/l No data given for Nominal and Measured Concentrations
Reference	:	Van Leeuven et al. (1990): Ecotox. Environ. Saf. 20, 42-52
Reliability	:	(2) valid with restrictions
14.09.2005		(131)
Species	:	Salmo gairdneri (Fish, estuary, fresh water)
Endpoint	:	other:embryolethality/ malformations/ weight of young fish
Exposure period	:	60 day(s)
Unit	:	mg/l
LC50	:	= 320
EC50	:	= 260
LOEC (60d)	:	32
Analytical monitoring	:	no data
Method	:	OECD Guide-line draft "Early Life Stage Test (ELS-Test)"
Year	:	1989
GLP	:	no data
Test substance	:	Other TS:
Test substance	:	Resorcinol ≥99%
Method	:	Methods used are described in VAN LEEUWEN, C. J., ESPELDOORN, A., AND MOL, F. (1986). Aquatic toxicological aspects of dithiocarbamates and related compounds. III. Embryolarval studies with rainbow trout (Salmo gairdneri). Aquat. Toxicol. 9, 129-145. Statistical Methods: Unfertilized eggs were excluded from the calculations and corrections were made for mortality in the controls in the statistical analyses. LC50 and 95% confidence intervals were calculated according to Litchfield and Wilcoxon (1949) or Kooyman (1981). If a test yielded concentrations without partial kills, the geometric mean of the 0 and 100% effect concentrations was taken as the LC50 and binomial confidence limits were calculated (Stephan, 1977). The same procedure was applied to the calculation of the EC50, after frequencies of embryonic mortality and abnormal development observed in the posthatch larvae were combined. Differences in mean survival and abnormal development under the experimental concentrations were tested against the blank control by means of a x^2 test (Sokal and Rohlf, 1981). Concentrations affecting survival by more than 50% were excluded from the statistical analyses as size-selective mortality might occur. Data on embryotoxicity of the species were compared by means of orthogonal regression analysis.
Test condition	:	Embryolarval tests with S. gairdneri were initiated with freshly fertilized eggs obtained from a fish hatchery at Vaassen (Gelderland, the Netherlands). About 3 hr after fertilization 100 eggs were transferred to 15-liter all-glass aquaria containing 10 liters of test solution made up in reconstituted water also prepared according to Alabaster and Abram (1965), but with a hardness of 50 mg/liter (as $CaCO_3$), a pH of 7.7 ± 0.2, and an oxygen concentration of 10.8 ± 0.2. The eggs were placed in a Petri dish (diameter 25 cm) on the bottom of the tanks. The tests were carried out in duplicate, in a constant-temperature room of 10 ± 1 °C. During embryogenesis the room was kept as dark as possible. After hatching, the eggs were exposed to a 12-hr photoperiod. The aquaria were regularly inspected for dead larvae, which were removed. The test media were renewed three times a week. The range between the concentrations was 3.2. The tests were terminated after 60 days. Surviving fish were anesthetized, and malformed and normal fish were separated. Wet weight of all fish and length of macroscopically normal fish were determined.
Remark	:	The rainbow trout test formed part of a larger study comparing the ELS

toxicity of zebra fish (7 days) and rainbow trout (60 days) with a view to using the zebra fish test as a short-cut method both for environmental hazard assessment and for screening of direct-acting human teratogens.

Result : EC50: 260 mg/l
LC50: 320 mg/l
LOEC (60d): 32 mg/l
No data given for Nominal and Measured Concentrations

Reference : Van Leeuven et al. (1990): Ecotox. Environ. Saf. 20, 42-52

Reliability : (2) valid with restrictions

14.09.2005 (131)

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Species	:	Daphnia magna (Crustacea)
Endpoint	:	other: survival rate/reproduction
Exposure period	:	21 day(s)
Unit	:	µg/l
NOEC	:	172 measured/nominal
LOEC	:	> 172 measured/nominal
EC50	:	> 172 measured/nominal
MATC	:	> 172 measured/nominal
Analytical monitoring	:	yes
Method	:	other: see remarks
Year	:	2003
GLP	:	yes
Test substance	:	other TS: see remark

Test substance : Resorcinol USP Grade Flake, Lot 15-1.
Purity 99.96%

Method : Conducted to:
OECD Guideline No. 211
FIFRA Guideline 72-4
OPPTS Draft Guideline 850.1300

Result : After 21 days of exposure, survival among the dilution water control organisms averaged 95%. The cumulative number of offspring released by each female organism of the dilution water control organisms during the 21-day test was 112 offspring per female. As demonstrated by the performance of the dilution water control, the exposure system provided conditions which were appropriate for promoting acceptable survival and reproduction of the test species and met the minimum standard criteria established by OECD guidelines (i.e., >= 80% survival and >= 60 offspring per female). The dilution water control organisms released their first brood of offspring on test day 10. Time of first brood release was within normal performance expectation for this species.

At termination of the test, survival of 95, 95, 95, 95 and 100% was observed among daphnids exposed to the 11, 35, 53, 111 and 172 µg a.i./L treatment levels, respectively, and was not statistically different compared to the control data (i.e., 95%). The 21-day EC50 for Daphnia magna survival and Resorcinol was empirically estimated to be > 172 µg a.i./L, the highest measured concentration tested.

Following 21 days of exposure, the organisms exposed to the 11, 35, 53, 111 and 172 µg a.i./L treatment levels had released a mean cumulative offspring per female of 125, 114, 127, 140 and 153, respectively, and was statistically similar to the control data (i.e., 112). First brood release by daphnids exposed to all treatment levels occurred on test day 10 and was consistent with the performance of the control organisms.

Mean total body length at test termination among daphnids exposed to the control averaged 4.7 mm per daphnid. Mean total body length among daphnids exposed to the 11, 35, 53, 111 and 172 µg a.i./L treatment levels, averaged 4.8, 4.7, 4.8, 4.9 and 4.9 mm, respectively, and was statistically similar to the control data (i.e., 4.7 mm).

Mean dry weight at test termination among daphnids exposed to the control averaged 0.95 mg per daphnid. Mean dry weight at test termination among daphnids exposed to the 11, 35, 53, 111 and 172 µg a.i./L treatment levels, averaged 0.97, 0.93, 0.99, 1.12 and 1.15 mg, respectively, and was statistically similar to the control data (i.e., 0.95 mg).

Cumulative mean percent survival of parental daphnids (Daphnia magna) during the 21-day chronic exposure to Resorcinol.

Mean Percent Survival (SD)	Treatment Level (µg a.i./L)					
Test Day	Control	25	50	100	200	400
1	100(0)	100(0)	100(0)	100(0)	100(0)	100(0)
2	100(0)	100(0)	100(0)	100(0)	100(0)	100(0)
3	100(0)	100(0)	100(0)	100(0)	100(0)	100(0)
4	100(0)	100(0)	100(0)	100(0)	100(0)	100(0)
5	100(0)	100(0)	100(0)	100(0)	100(0)	100(0)
6	100(0)	100(0)	98(5)	98(5)	100(0)	100(0)
7	100(0)	100(0)	98(5)	98(5)	100(0)	100(0)
8	100(0)	100(0)	98(5)	98(5)	100(0)	100(0)
9	100(0)	100(0)	98(5)	98(5)	100(0)	100(0)
10	100(0)	100(0)	95(6)	98(5)	98(5)	100(0)
11	100(0)	100(0)	95(6)	98(5)	98(5)	100(0)
12	100(0)	98(5)	95(6)	98(5)	95(6)	100(0)
13	100(0)	98(5)	95(6)	98(5)	95(6)	100(0)
14	100(0)	98(5)	95(6)	98(5)	95(6)	100(0)
15	100(0)	98(5)	95(6)	98(5)	95(6)	100(0)
16	100(0)	98(5)	95(6)	98(5)	95(6)	100(0)
17	95(10)	98(5)	95(6)	95(6)	95(6)	100(0)
18	95(10)	98(5)	95(6)	95(6)	95(6)	100(0)
19	95(10)	95(6)	95(6)	95(6)	95(6)	100(0)
20	95(10)	95(6)	95(6)	95(6)	95(6)	100(0)
21	95(10)	95(6)	95(6)	95(6)	95(6)	100(0)

Cumulative mean number of offspring produced per daphnid (Daphnia magna) during the 21-day chronic exposure to Resorcinol.

Mean Cumulative Number of Offspring per Female (SD)	Treatment Level (ug a.i./L)					
Test Day	Control	25	50	100	200	400
10	14(2)	12(3)	11(2)	11(3)	20(5)	18(4)
13	26(2)	29(5)	26(6)	27(2)	31(2)	34(3)
15	42(7)	53(1)	46(7)	50(1)	55(8)	63(7)
17	59(5)	70(11)	67(10)	73(13)	97(11)	111(10)
20	88(5)	93(7)	90(9)	95(7)	106(16)	123(10)
21	112(4)	126(11)	114(13)	127(18)	140(17)	153(17)

Nominal test concentrations: 25, 50, 100, 200 and 400 µg/l
Mean measured concentrations: 11, 35, 53, 111 and 172 µg/l

Test condition : Test conditions:
21 day duration, 19 to 21°C, illumination of 16 hours light: 8 hours darkness

at 35 to 75 footcandles (380 to 810 lux).

Dilution water:
Fortified well water
ph: 8.0 to 8.2
Specific conductivity: 500 µmhos/cm
Total hardness as CaCO3: 160 mg/l
Total alkalinity as CaCO3: 110 mg/l

The adult daphnids used to produce offspring for this test (1) did not contain ephippia, (2) produced offspring prior to being 12 days old, (3) produced an average of 10.3 offspring per female per day seven days prior to test initiation, (4) were not used in any portion of a previous test and (5) survival was > 99%, 48 hours prior to test initiation.

At the initiation of the definitive study, Daphnia magna (≤ 24 hours old) were impartially selected and distributed to 24 unlabeled intermediate vessels (100 ml beakers) containing dilution water and several drops of algal food solution. The daphnids were impartially added, two at a time to each intermediate vessel, until each vessel contained two organisms. This process was repeated until each intermediate vessel contained ten organisms. The daphnids were then introduced into the replicate exposure vessels by impartially selecting one of the unlabeled intermediate vessels containing ten organisms and gently pipetting them one at a time under the surface of the test solution. This process was repeated until the test concentrations and the controls contained forty Daphnia magna (10 organisms per replicate vessel). Food solutions were added to the exposure solutions prior to the introduction of daphnids.

During culture, parental daphnids were fed 2.0 ml of a unicellular green algae (Ankistrodesmus falcatus) and 0.5 ml of YCT suspension (yeast, cereal leaves and digested flaked fish food) per test vessel once daily. The food solution contained approximately 4 x 10^7 cells/ml of algae. Test diet consisting of a suspension of green algae (Ankistrodesmus falcatus; 4 x 10^7 cells/ml), introduced at a rate of 3.0 ml of algal suspension and 1.0 ml of YCT suspension (yeast, cereal leaves and digested flaked fish food) per test vessel, three times daily.

1. Significant differences in the percent survival were evaluated after transformation (e.g., arcsine square-root percentage) of the data.
2. The Chi Square and Shapiro Wilks' Test, Kruskal Wallis' Test, Dunn's Test (Sokal and Rohlf, 1981) or Steel's One-Many Rank Test (Weber et al., 1989)
3. Hartley's Test and Bartlett's Test (Sokal and Rohlf, 1981).
5. Williams' Test (Williams, 1971, 1972) or Dunnett's Test.

There were no protocol deviations recorded.

Reference : Lima (2004): Resorcinol - Full life Cycle Toxicity Test with Water Fleas, Daphnia magna Under Flow-through conditions. Lab ID Number: Springborn Smithers Study No. 13048.6404

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

14.09.2005 (77)

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

Species	:	Lactuca sativa (Dicotyledon)
Endpoint	:	growth
Exposure period	:	3 day(s)
Unit	:	mg/l
EC50	:	ca. 200
EC37	:	ca. 100
EC75	:	ca. 400
Method	:	other: no data
Year	:	1976
GLP	:	no data
Test substance	:	Other TS: see remark
Test substance	:	Resorcinol sourced from J.T. Baker Chemical Co.
Method	:	Resorcinol has been identified as one of the degradation products of corn and rye. Chromatographic bioassay for phytotoxic activity of resorcinol to lettuce. Test parameter: Inhibition of root elongation No information given on method of application.
Test condition	:	Test substance concentrations: 25, 50, 75, 100, 200, 300 ppm (aqueous solution) Test conditions: 21-22°C
Result	:	Resorcinol significantly reduced growth at 100 ppm. Results were expressed as the percent radicle growth of the control: 100ppm = 63% (EC37 ca 100ppm) 200ppm = 49% (EC50 ca 200ppm) 300ppm = 41% 400ppm = 25% (EC75 ca 400ppm)
Reference	:	Identification and Phytotoxic Activity of Compounds Produced uring Decomposition of Corn and Rye Residues in Soil Chang-Hung Chou and Z.A. Patrick, Institute of Botany, Academia Sinica, Taipei, Republic of China and Department of Botany, University of Toronto, Toronto, Canada
Reliability	:	(4) not assignable No data on purity, no data on GLP, no data on method

14.09.2005 (18)

Species	:	other terrestrial plant: Atriplex triangularis (Halophytes)
Endpoint	:	other: Inhibition of Germination
Exposure period	:	20 day(s)
Unit	:	mg/l
EC93	:	= 1100
Method	:	other: no data
Year	:	No data
GLP	:	no data
Test substance	:	no data
Remark	:	20 days exposure of seeds of the halophytic plant to 1.1 g resorcinol/l water (Tween 20 used as solubilizer) caused 93% inhibition of germination relative to control.
Reliability	:	(4) not assignable

14.09.2005 (69)

Species	:	other terrestrial plant: Chick-pea plants
Endpoint	:	No data
Exposure period	:	No data
Unit	:	mg/l

Remark	:	Chick-pea plants were sprayed at the start of blossoming and 15 days later with solutions of resorcinol (5, 20 and 50 mg/l). In comparison with the control cultures, the number of the pods per plant at the middle concentration was strongly increased. The number of peas per pod was reduced at the lowest concentration. The weight of one thousand peas and the yield per hectare were greater than in reference cultures. The content of soluble protein and soluble sugars was also higher and the content of free amino acids and starch only greater than in the reference cultures at the low concentration.
Reliability	:	(4) not assignable
14.09.2005		(80)

Species	:	other terrestrial plant: Pea plants (Cajanus cajan (L.) Millsp.)
Endpoint	:	No data
Exposure period	:	No data
Unit	:	mg/l
Remark	:	Pea plants (Cajanus cajan (L.) Millsp.), which were sprayed with resorcinol (500 l/ha; concentration 100 mg/l) 70 and 77 days after having been planted had 17% more blossoms per plant relative to the control and 9% more pods.
Reliability	:	(4) not assignable
14.09.2005		(114)

Species	:	other terrestrial plant: Imatiens balsamina
Endpoint	:	No data
Exposure period	:	No data
Unit	:	mg/l
Remark	:	In studies conducted in Imatiens balsamina, a spring cabbage, 4 out of 10 plants (control:0) managed to blossom despite 25 applications (3 drops every 2 days to a cotton bud located around the growing tip of the plant) of resorcinol (10 mg/l) and 24 hours exposure to light every day. At 8 hours light exposure every day, even the control plants became active: however, the resorcinol-treated plants formed more buds more rapidly.
Reliability	:	(4) not assignable
14.09.2005		(68)

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

Type	:	Artificial soil
Species	:	Eisenia fetida (Worm (Annelida), soil dwelling)
Endpoint	:	Mortality and growth
Exposure period	:	42 day(s)
Unit	:	mg/kg soil dw
LC100	:	ca. 40000
Method	:	Other: see remark
Year	:	1982
GLP	:	no data
Test substance	:	Other TS:
Test substance	:	Supplied from Aldrich Chemical Co., Milwaukee, WI
Test condition	:	24 degree C
Method	:	The test substance was processed for assay by mixing 0.01, 0.05 or 1.0 g into 100 g sludge which contained 11-15% solids. Assuming exactly 13% solids in the sludge, the substance was thus tested at concentrations of about 0, 0.1, 1.0, 4 and 8% (w/w) dry wt, including comtrols. About 30 g sludge (ca. 13% solids) with test substance were placed over a ca. 4 mm depth of silt loam in a 20 x 100 mm Petri dish. Two hatchlings,

each under 10 mg live, wt, were added. The set of 25 dishes with 5 replicates of 5 concentrations was then stored at 24 ± 1°C. Growth was checked every 2 weeks and worms were transferred to freshly prepared substance at 4 weeks. Growth achieved at 2 or 4 weeks was determined by rinsing the worms in distilled water, blotting and weighing. Weight at 6 weeks was evaluated by analysis of variance. Significant differences were determined by the Neulman-Keul test (Zar, 1974).

Mortality was determined by enumeration and said to be significant if 5 or more earthworms died.

Result : Hatchlings in control dishes could gain more than 500 mg in 6 weeks. An average weight of 582 mg ± 85 SD, with a coefficient of variation of 14.6%, was attained by controls in 6 weeks in 45 similar assays during 16 months. This reflects both variation in earthworm growth and sludge quality. Mortality among controls was less than 2%.

The test substance did not permit the worms to grow more rapidly and achieve greater weight than was obtained in the controls. Resorcinol caused significant mortality at 4% in sludge (w/w) dry weight.

LC100: 40000 mg/kg soil dw
LOEC: 10000 mg/kg soil dw

Reference : Hartenstein (1982): Soil Biol. Biochem. 14, 595-599
Reliability : (4) not assignable
14.09.2005 (43)

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

Species	:	other not soil dwelling arthropod: Lasioderma serricorne
Endpoint	:	mortality
Exposure period	:	69 day(s)
Unit	:	ppm
LC70	:	= 100000
Method	:	No data
Year	:	1990
GLP	:	no data
Test substance	:	Other TS:
Test substance	:	Supplied by Aldrich Chemical Co.
Remark	:	Larvae and adult animals of the beetle Lasioderma serricorne, which live in symbiosis with an intracellular yeast, received resorcinol (10%) with their feed. After 14 and 26.6 days exposure, the mortality rate was 70% (control after 14 days exposure: 0). In the case of aposymbiotic insects (free from the intracellular symbiotic yeast), the mortality rate after 61.8 days exposure was 70%.
Reliability	:	(4) not assignable

14.09.2005 (29)

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

In Vitro/in vivo	:	In vivo
Type	:	Absorption, Metabolism and Excretion
Species	:	Rat
Number of animals		
Males	:	3
Females	:	3
Doses		
Males	:	112 and 225 mg/kg
Females	:	112 and 225 mg/kg
Vehicle	:	other: corn oil (oral administration), saline (iv injection)
Route of administration	:	Gavage and iv injection
Exposure time	:	5 day(s)
Product type guidance	:	No data
Decision on results on acute tox. Tests	:	No data
Adverse effects on prolonged exposure	:	No data
Half-lives	:	1st: No data 2nd: No data 3rd: No data
Toxic behaviour	:	No data
Deg. product	:	Glucuronide conjugate of resorcinol
Method	:	Other
Year	:	1987
GLP	:	No data
Test substance	:	other TS:

Test substance : ^{14}C radiolabelled test substance. Radiochemical purity: 97%; Non-radioactive resorcinol purity: > 99%

Method : In-house method to determine comparative metabolism and resorcinol in male and female F344 rats. The study was undertaken in two parts: disposition study and repeated exposure.

For the disposition study, groups of rats were treated by oral administration of 112 or 225 mg/kg of ^{14}C Resorcinol and sacrificed by carbon dioxide asphyxiation either 4, 8, 12, 16, 20 or 24 hours later and immediately dissected. Samples of each of the major tissues were taken, weighed, and stored at -20°C until assayed.

For the repeated exposure study, rats of both sexes were treated by oral administration of 225 mg/kg of ^{14}C Resorcinol for 5 consecutive days.

Male and female Fischer 344 rats (150 -170 g; obtained from Charles River Breeding Laboratories, Raleigh CA) were housed at room temperature in individual metabolism cages for separate collection of urine and feces. Rat urine was collected in a vessel submerged in dry ice to minimize the possible breakdown of metabolites. Water and pelleted NIH 31 rat chow were provided *ad libitum*. Radiolabeled resorcinol was diluted with unlabeled resorcinol to administer approximately 5 μCi per rat. For oral administration, corn oil was used as a vehicle and saline was used for iv treatment.

^{14}C radioactivity in each tissue was analyzed by combustion of triplicate 50- or 100-mg samples to $^{14}CO_2$ on a Packard TriCarb sample oxidizer The $^{14}CO_2$ was counted with liquid scintillation counter. Samples of urine (0.02 ml) were counted directly without combustion." Body composition estimates for blood and muscle were 8 and 50%, respectively (Matthews and Anderson, 1975), and for adipose tissue and skin, 11 and 16%, respectively (Birnbaum *et al.*, 1980). All other tissue volumes were

determined gravimetrically. Fecal samples were air dried, weighed, and ground to a fine powder with a mortar and pestle before the radioactivity was determined.

CO_2 collection.
Following oral administration of [^{14}C] resorcinol, each rat was placed in a Metabowl Mark III glass metabolism cage (Jencons Ltd., Hemel Hemstead, Hertfordshire, England) maintained at an air flow rate of 0.4 to 0.5 liters/min. Total air flow through the cage was passed through an ethanol (200 ml) trap for collection of volatiles and then through 200 ml of 2-methoxyethanol: ethanolamine mixture (7:3) for $^{14}CO_2$ collection. The percentages of the total dose of [^{14}C] resorcinol eliminated as $^{14}C0_2$ and volatiles were determined by counting triplicate 1-ml aliquots of each trapping solution.

Biliary excretion.
Excretion of [^{14}C] resorcinol-derived radioactivity in the bile was determined in rats anesthetized with pentobarbital 50 mg/kg ip and 50 mg/kg po (Matthews, 1978). After the common bile duct was cannulated, [^{14}C] resorcinol was injected into a femoral or tail vein and serial bile samples were collected for 6 hr. The radioactivity in each sample was determined by liquid scintillation counting of triplicate l0-µl aliquots.

Metabolism of resorcinol.
The metabolites and parent compound in the urine were analyzed by HPLC equipment attached to a Flow-One/Beta Model CT radioactive flow detector

Enzymatic and acid hydrolysis of metabolites in urine.
Radioactivity excreted in urine was subjected to enzymatic or acid hydrolysis. For enzymatic digestion, the incubation mixture contained urine and ß-glucuronidase, or arylsulfatase in sodium acetate buffer . D-Saccharic acid 1,4-lactone was added to inhibit ß -glucuronidase activity in the arylsulfatase preparation. Similar incubations minus enzyme, served as controls. All incubations were carried out at 37°C for 15 hr. The resulting hydrolysates were analyzed by HPLC.

Data analysis.
A two-tailed Student's *t* test was used to compare the difference between male and female rats.

Result : The test substance was readily absorbed from the gastrointestinal tract, rapidly metabolized and excreted by male and female rats. In both sexes, most of the dose (> 90%) was excreted in the urine within 24 hours after oral administration of 112 mg/kg, indicating little potential for bioaccumulation in animal tissues. Less than 3% of an oral dose was excreted in the faeces. An analysis of bile indicated that at least 50% of the dose excreted in bile undergoes enterohepatic circulation to be eventually excreted in urine. Little (<5%) of the parent compound was excreted in urine; most of the dose was in the form of three major and one minor metabolite. The relative amounts of metabolites excreted changed only slightly with time and dose administered. Approximately 70% of the total radioactivity in the urine of both sexes was in the form of glucuronide conjugate. Female rats excreted a greater portion of the dose as a sulfate conjugate than males. Males excreted more of a diconjugate both sulfate and glucuronide groups. Repeated exposure to up to five daily doses resulted in no apparent alteration of the pattern of absorption, metabolism and excretion observed after a single dose.

Reference : Comparative Metabolism and Excretion of Resorcinol in Male and Female F344 Rats
Kim, Matthews (1987): Fund. Appl. Toxicol. 9, 409-414

Reliability : (1) valid without restrictions
14.09.2005

(70)

In Vitro/in vivo	:	In vivo
Type	:	Metabolism
Species	:	rat
Number of animals		
Males	:	25
Females	:	0
Doses		
Males	:	100 mg/kg
Females	:	-
Vehicle	:	water
Route of administration	:	s.c.
Exposure time	:	30 day(s)
Product type guidance	:	No data
Decision on results on acute tox. tests	:	No data
Adverse effects on prolonged exposure	:	No data
Half-lives	:	1st: No data 2nd: No data 3rd: No data
Toxic behaviour	:	None
Deg. product	:	Yes
Method	:	Other: see remark
Year	:	1982
GLP	:	no data
Test substance	:	Other TS:

Test substance : ^{14}C radiolabelled resorcinol

Method : To select the dose levels for the pharmacokinetic excretion and tissue distribution studies, male rats (Charles River, COBS, CD(SD)), weighing 269 to 352 g, were divided into 5 groups of 5 rats each. Animals were injected subcutaneously with doses of resorcinol of 55, 88, 140, 220 and 350 mg/kg. The animals were then observed for treatment-related effects.

Pharmacokinetic studies were performed with groups of adult, male Sprague-Dawley rats weighing 200-250 g. They were given a single subcutaneous dose of resorcinol (10 or 50 or 100 mg/kg) containing trace amounts of ^{14}C resorcinol. Two or three rats were sacrificed at 1, 3, 6 and 24 hours after injection for the collection of blood and specimens of kidney, liver, brain, intestines, spleen, and muscle. Urine and feces were obtained when available. Retro-orbital blood was collected from the rats at early and intermediate times after dosing.

For multiple-dose studies, rats were treated daily with unlabeled resorcinol at a total dose of 100 mg/kg, given subcutaneously in two divided doses of 50 mg/kg, each given 6 hours apart. After 14 days and 30 days of treatment, groups of rats were injected with a single 50 mg/kg dose of resorcinol containing trace amounts of ^{14}C-resorcinol. Then, 3 rats were sacrificed 1, 3, 6 and 24 hours after injection for the collection of tissues, blood, feces and urine. Blood samples also were obtained from the retro-orbital sinus at intervals of 15 minutes for the first hour, and at 2, 3, and 6 hours.

All tissues and organs were preweighed. Two sections from different areas were obtained and digested in 2.0 ml of PROTOSOL® tissue solubilizer at room temperature for at least 48 hours; a few drops of 30% hydrogen peroxide solution were added for discoloration and the radioactivity was measured by scintillation counting. Samples of feces and intestinal contents were homogenized with 10-15 ml of water and the radioactivity was then determined by counting. The urine and plasma samples were analysed by TLC and autoradiography before and after enzymatic hydrolysis. GC/MS was used for final confirmation of the molecular structure of the metabolites. Standard error of the means (S.E.M) was

estimated from the range (Mantel, 1951).

Result : In the dose selection studies, no gross toxic signs were observed at 55 and 88 mg/kg dose levels. Slight tremors, which progressed to moderate to marked tonic clonic convulsions, occurred with 10 minutes following doses ≥ 140 mg/kg. Complete recovery occurred in all animals so affected by 1 – 1.5 hours following dosing. On basis of these observations, 100 mg/kg was selected as the maximum dose for the pharmacokinetic studies.

This total daily dose, given as two 50 mg/kg subcutaneous injections over a 30 day period did not result in any overt toxic signs or adverse changes in body weight gain, organ weight (liver, kidney, brain, spleen and testes), hematocrit, hemoglobin, red blood cell count and serum T_3 and T_4. Additional, histopathology was judged to be within normal limits for the three organs examined: thyroid gland, spinal cord and brain.

Repeated dosing for 30 days with maximum tolerated daily doses of 100 mg/kg did not alter pharmacokinetic parameters, nor cause overt toxic signs or adverse reactions. The animals body weight, blood values, levels of serum T3 and T4 and the gross microscopic appearance of the thyroid gland and spinal cord remained within normal limits.

Reference : Merker et al. (1982): Res. Commun. Chem. Pathol. Pharmacol. 38, 367-388

Reliability : (2) valid with restrictions
No data on purity, no data on GLP

14.09.2005 (88)

In Vitro/in vivo : In vivo
Type : Absorption
Species : Human
Number of animals
Males : 3
Females : 0
Doses
Males : 12 mg/kg/day
Females : -
Vehicle : other:hydroalcohol
Route of administration : dermal
Exposure time : 28 day(s)
Product type guidance : No data
Decision on results on acute tox. tests : No data
Adverse effects on prolonged exposure : No data
Half-lives : 1st: No data
2nd: No data
3rd: No data
Toxic behaviour : No data
Deg. product : No data
Method : No data
Year : 1983
GLP : no data
Test substance : No data

Result : The adsorption and metabolic disposition of 2% resorcinol applied topically in a hydroalcoholic vehicle was determined in three human subjects. The test substance penetrated the skin at a rate of 0.37 µg/cm^2/hour. After two weeks of application of 800 mg resorcinol to about 30% of body surface of each subject, an average of 1.64% of the dosage was being excreted in 24-hour urine specimens as the glucuronide or as the sulfate conjugate. There was no resorcinal in blood drawn at weeks 1, 2, 3 and 4 nor were there any abnormalities in thyroid function or blood chemistries at weeks 2, 3 and 4.

Reliability : (2) valid with restrictions

14.09.2005 (142)

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	202 mg/kg bw
Species	:	rat
Strain	:	Wistar
Sex	:	female
Number of animals	:	10 per dose
Vehicle	:	other: A 5% suspension in 2% thin paste of starch used for various doses
Doses	:	100, 160, 250, 400, 630 mg/kg
Method	:	other:In house method
Year	:	1979
GLP	:	no
Test substance	:	Other TS: see remark

Test substance : Nako-Brown 3G, brown-gray powder

Method : The test substance was prepared as 5% suspension in 2% thin paste of starch (5 g/ad 100 ml) and administered in various single doses by a stomach tube to female Wistar rats (strain: Hoe WISKf(SPF71); own breed) weighing 182 to 224 g. Ten rats were exposed per dose. For 16 hours before and 2 hours after, food was withheld from the animals. During the subsequent 14-day observation period following administration, the animals received the maintenance diet ALTROMIN 1324 as their feed and tap water ad libitum. The animals were kept in groups in plastic cages on wood shavings.

After exposure, clinical signs, mortality rate and median lethal time were recorded. In the subsequent observation period, the animals were weighed on a weekly basis. Lethally intoxicated animals were dissected and the macroscopic dissection findings recorded. At the end of the observation period, the surviving test animals were sacrificed with CO_2 gas, dissected and also examined macroscopically.

The LD50 was determined by means of Probit analysis (LINDER and WEBER method); the confidence limits were calculated according to CAVALLI-SFORZA (program prepared by the Department of Practical Mathematics of Hoechst Aktiengesellschaft).

Results : At the end of the 14-day observation period the following mortality rates were determined at the various doses:

Dose mg/kg	Concentration %	Number of Dead Animals/ Number of Animals Used
100	5	0/10
160	5	4/10
250	5	7/10
400	5	9/10
630	5	10/10

Lethally-intoxicated animals died between 16 minutes and 11 days after administration with the following clinical symptoms: motor difficulties, squatting, ruffled fur, enlarged palpebral fissure, decubitus position, passivity, shivering, twitching, tonic-clonic seizures, miosis, increased tearing, cyanosis, elevated respiratory frequency and irregular superficial breathing. The surviving test animals showed the same symptoms in milder form and were symptom-free 24 hours post-application.

Behavior and trends in body weight were normal during the observation period.

Dissection of the sacrificed animals showed macroscopically brown-dyed stomach walls. The stomachs were filled with a dark brown to black substance and the small intestine with a lightbrown to orange substance. Dissection of the animals sacrificed at the end of the test showed no particular macroscopic findings.

At the end of the 14 days observation period an LD50 of 201.9 mg/kg body weight (163.8 –248.9) was determined by means of Probit analysis.

Reference : Hoechst AG (1979):Acute Oral Toxicity of Nako-Brown 3G in female rats(Report number 171/79)

Reliability : (2) valid with restrictions
14.09.2005 (51)

Type : LD50
Value : = 980 mg/kg bw
Species : rat
Strain : no data
Sex : male
Number of animals : 5
Vehicle : water
Doses : 0.398 – 3.16 g/kg
Method : other: Federal Register of August 12, 1961 pages 7333-7341
Year : 1962
GLP : No data
Test substance : other TS:

Test substance Flaked and Industrial Grade Resorcinol

Method : The study was conducted in accordance with Federal Hazardous Substances Labeling Act (FHSLA), Federal Register Aug. 12, 1961, p 7333-7341, Part 191 "Hazardous Substances Definitions and Procedural and Interpretative Regulations, Final Order".

The following doses: 398, 795, 1580 and 3160 mg/kg of flaked and industrial grade resorcinol were administered by stomach intubation to groups of 5 non-fasted male albino rats weighing between 200-300 g. The concentration of the material in water was adjusted for the various dosage level groups so that no less than 1. 0 milliliter of the mixture was administered to any rat at the lowest level and no more than 10 milliliters at the highest level. The rats were observed for 14 days at which time mortality due to chemical exposure was considered complete. All fatalities were subjected to autopsies to exclude extraneous causes of death. Survivors were sacrificed and examined for existence of gross lesions. The single dose oral LD50, based upon mortality during the 14-day observation period, was estimated by Thompson's method of moving averages using the tables of Weil.

Results :

Dosage mg/kg	No. Died/No. Dosed	Days after dosing on which death occurred
398	0/10	-
795	1/5	<3 hr (1)
1580	5/5	<2-3 hr (5)
3160	5/5	<2 hr (5)

95% confidence limits: 740-1290 mg/kg.

All of the rats which died during the observation period revealed hyperemia and distention of stomach and intestines upon autopsy. The majority of the rats which survived the observation period showed body weight gains within significant limits of those of control rats. None of the rats sacrificed following the holding

period exhibited any gross lesions upon pathological examination.

Reference : Range Finding Toxicity Tests on Flaked Grade Resorcinol; Industrial Hygiene Foundation of America Inc., Oct-Dec 1962 (conducted by Koppers Company)
Reliability : (2) valid with restrictions
13.09.2005 (103)

Type : LD50
Value : 301 mg/kg bw
Species : rat
Strain :
Sex : male
Number of animals : 5
Vehicle : water
Doses : 147, 215, 316, 464 mg/kg
Method : other:no data
Year : 1970
GLP : no data
Test substance : Other TS: Resorcinol Powder

Result : LD50 95% confidence limits: 213 - 426 mg/kg

Mortalities:

Dose mg/kg	No. of deaths	Time of death
147	0/5	N/A
215	1/5	0-4 hours
316	3/5	0-4 hours
464	4/5	0-4 hours

Clinical signs:
Clinical signs of fibrillation, tremors, convulsions, salivation, dyspnea, sedation, and emaciation were observed in all treatment groups.

Gross autopsy:
No significant findings were observed during the gross autopsy of survivors.
In decendants there were gross autopsy findings of hemmorhage of lungs, inflammation of gastrointestinal tract and hyperemia of liver.

Reliability : (2) valid with restrictions
14.09.2005 (60)

5.1.2 ACUTE INHALATION TOXICITY

Type :
Value :
Species : Rat
Strain : Harlan-Wistar
Sex : Female
Number of animals : 6
Vehicle : Distilled water
Doses : 2,00 mg/M^3
Route of admin. : Inhalation
Exposure time : 1 hour and 8 hours
Method : Other : see remark
Year : 1976
GLP : No data
Test substance : Other TS:

Test substance : Resorcinol Flake

Method		The acute toxic effects of catechol-, resorcinol- and phenol-water aerosols were investigated at comparable airborne concentrations. Samples were dissolved in distilled water and the resulting solutions were aerosolized using a D18 Dautrebande aerosol generator operated at 30 psi. At this operating pressure, the D18 generator delivered droplets of 1µ or smaller. The concentration of the sample solutions was adjusted so that the airbourne concentration approximated 2,000 mg/M^3 of the sample in air. Airborne concentrations were determined by measurement of the volume loss of solution following aerosolization. The weight of sample present in that volume was then calculated and related to the total volume of air in generating the aerosol to obtain chamber concentrations. In groups of 6, rats, weighing between 87 and 126 g, were subjected to a single 1 hour or 8 hour inhalation period of the aerosolized sample. The animals were held for 14 days following exposure and were then weighed and sacfrificed for gross autopsy.
Result		No deaths resulted when rats inhaled resorcinol-water aerosols for one-hour or eight hour time periods at concentrations of 2,130 mg/M^3 and approx 7,800 mg/M^3 for a 1 hour period, or concentrations of 2,000 to 2,800 mg/M^3 for an 8 hour period. All animals had normal 14-day weight gains, and no lesions attributable to inhalation of the aerosol were seen at gross autopsy.
Conclusion	:	No toxic effects are anticipated from the infrequent inhalation of resorcinol at aerosol concentrations approximating 2,000 mg/M3.
Reference	:	The benzenediols: catechol, resorcinol and hydroquinone – a review of the industrial toxicology and current industrial exposure limits C.W. Flickinger, Manager, Industrial Hygiene & Safety Group, Koppers Company Inc., Research Department, Monroeville, Pennsylvania 15146, USA, Am. Ind. Hyg. Assoc. J. 37, 596-606
Reliability 14.09.2005	:	(4) not assignable (37)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Value	:	= 3360 mg/kg bw
Value		= 2830 mg/kg bw
Species	:	rabbit
Strain	:	No data
Sex	:	Male
Number of animals	:	4
Vehicle	:	physiol. saline
Doses	:	4000 mg/kg
Method	:	other: Federal Register of August 12 1961, pages 7333-7341
Year	:	1962
GLP	:	No data
Test substance	:	Other TS:
Test substance	:	Flaked and Industrial Grade Resorcinol
Method	:	The study was conducted in accordance with Federal Hazardous Substances Labeling Act (FHSLA), Federal Register Aug. 12, 1961, p 7333-7341, Part 191 "Hazardous Substances Definitions and Procedural and Interpretative Regulations, Final Order" Four male albino rabbits were used, weighing between 2.3-3.0 kg after undergoing a seven day laboratory observation and acclimatization period. The rabbits were administered the following doses of flaked and industrial resorcinol: 1000, 2000, 3980 and 7950 mg/kg. Prior to exposure, the

animals were prepared by clipping the skin of the trunk, approximately 10% of the body surface, free of hair. One-half of each group was further prepared by making epidermal abrasions every two or three centimeters longitudinally over the area of future exposure. The abrasions were sufficiently deep to penetrate the stratum corneum but not to disturb the derma and cause bleeding. The skin and the material, which was evenly distributed on cotton gauze in an amount calculated to yield the desired dosage level, were moistened with physiological saline. The gauze and material were applied to the skin of the rabbits and the entire trunk was wrapped in an impervious plastic film. The maximum justifiable dosage level for solids in this procedure is approximately 4. 0 gm. /kg. which is twice the upper limit for the "toxic substance" category as defined in the regulations pursuant to the FHSLA. Following dosing, the rabbits were immobilized in stocks for 24 hours after which the dam and any excess chemical were removed and the skin was examined for gross changes. Mortality due to the effect of the chemical was considered complete after 14 days. All fatalities were subjected to autopsies to exclude extraneous causes of death while some survivors were sacrificed and examined for the existence of gross lesions.
The skin penetration LD50, based upon mortality attributable to the material during the 14-day observation period, was estimated employing Thompson's method of moving averages using the tables of Weil.

Result : Flaked Grade:

Dosage g/kg	No. Died/No. Dosed	Days after dosing on which death occurred
1.00	0/4	-
2.00	1/4	1 (1)
3.98	2/4	1 (2)
7.95	4/4	1 (4)

95% confidence limits: 1980-5710 mg/kg.

Industrial Grade:

Dosage g/kg	No. Died/No. Dosed	Days after dosing on which death occurred
1.00	0/4	-
2.00	0/4	-
3.98	4/4	1 (4)
7.95	4/4	1 (4)

95% confidence limits: cannot be calculated due to the all or none response.

The material produced necrosis of the skin in all the rabbits exposed to 3980 mg/kg and above for the Flaked Grade and to 2000 mg/kg and above for the Industrial Grade. The rabbits exposed to 1000 mg/kg Flaked Grade showed only slight hyperkeratosis following signs of moderate to severe irritation after 24 hours contact. However the same dose of the Industrial Grade showed no signs of irritation seven days following contact. The majority of the rabbits that survived the 14-day observation period exhibited body weight gains significantly less than those of control rabbits. No internal gross lesions were observed at autopsy.

Reference : Range Finding Toxicity Tests on Flaked Grade Resorcinol; Industrial Hygiene Foundation of America Inc., Oct-Dec 1962 (conducted by Koppers Company)

Reliability : (2) valid with restrictions
No data on GLP

5.1.4 ACUTE TOXICITY, OTHER ROUTES

Type	:	LC50
Value	:	= 215 mg/kg bw
Species	:	mouse
Strain	:	No data
Sex	:	Male
Number of animals	:	No data
Vehicle	:	No data
Doses	:	No data
Route of admin.	:	i.p.
Exposure time	:	No data
Method	:	Other: no data
Year	:	1966
GLP	:	no data
Test substance	:	no data

Reliability : (4) not assignable
14.09.2005 (98)

Type	:	LC50
Value	:	450 mg/kg bw
Species	:	rat
Strain	:	No data
Sex	:	No data
Number of animals	:	No data
Vehicle	:	No data
Doses	:	No data
Route of admin.	:	s.c.
Exposure time	:	No data
Method	:	no data
Year	:	No data
GLP	:	no data
Test substance	:	no data

Reliability : (4) not assignable
14.09.2005 (119)

Type	:	LC50
Value	:	213 mg/kg bw
Species	:	mouse
Strain	:	No data
Sex	:	No data
Number of animals	:	No data
Vehicle	:	No data
Doses	:	No data
Route of admin.	:	s.c.
Exposure time	:	No data
Method	:	no data
Year	:	No data
GLP	:	no data
Test substance	:	no data

Reliability : (4) not assignable
14.09.2005 (81)

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	500 mg
Exposure	:	Abraded and intact skin
Exposure time	:	24 hour(s)
Number of animals	:	6
Vehicle	:	physiol. saline
PDII	:	4.4
Result	:	Not irritant
Classification	:	None
Method	:	Other: see remark
Year	:	1962
GLP	:	No data
Test substance	:	Other TS:

Test substance : Flaked and Industrial Grade Resorcinol

Method : This study was conducted in accordance with Federal Hazardous Substances Labeling Act (FHSLA), Federal Register Aug. 12, 1961, p 7333-7341, Part 191 "Hazardous Substances Definitions and Procedural and Interpretative Regulations, Final Order".

Flaked Grade (deep, ivory colored solid) and Industrial Grade (dark brown colored solid), no purity data available.

The irritation produced by a single contact of each material with the skin was measured by a patch-test technique on the abraded and intact skin of male, albino rabbits, clipped free of fur. One-half of a gram of the material was moistened with physiological saline and applied, under one-inch-square gauze patches to three intact and three abraded areas randomly distributed over the bellies of six male, albino rabbits. The patches were secured in place by adhesive tape and the trunks of the animals were wrapped in impervious plastic films to further secure the patches and retard the evaporation of the chemical. Following a 24-hour period of exposure, during which the rabbits were confined in stocks, the patches were removed and the skin reactions were evaluated on the basis of erythema, edema, and necrosis. The exposed areas were again evaluated after 72 hours. Areas of the skin which were damaged by the material were kept under observation for a maximum period of two weeks.

Results : Flaked Grade:

Evaluation Time (hours)	Effect on skin			
	Erythema		Edema	
	A. Intact	B. Abraded	C. intact	D. Abraded
24	0.7	2.7*	1.3	3.0*
72	1.2	3.5*	1.5	3.5*
Total	1.9	6.2*	2.8	6.5*

Primary Irritation score [(A+B+C+D)/4]: 4.4
*Based upon necrotic areas being scored 4.0, the maximum score possible, for both eythema and edema.

Industrial Grade:

Evaluation Time (hours)	Effect on skin			
	Erythema		Edema	
	A. Intact	B. Abraded	C. intact	D. Abraded
24	2.2	3.7*	1.8	4.0*
72	2.0	4.0*	0.0	4.0*
Total	4.2	7.7*	1.8	8.0*

Primary Irritation score [(A+B+C+D)/4]: 5.4

*Based upon necrotic areas being scored 4.0, the maximum score possible, for both eythema and edema.

The contact of 0. 5 gm of the test material with the intact and abraded areas of the skin of male, albino rabbits for a maximum period of 24 hours produced responses, the most severe of which were:
Intact, moderate irritation; Abraded, necrosis; primary irritation score, 4. 4 for the Flaked Grade.
Intact, severe irritation; Abraded, necrosis; primary irritation score, 5.4 for the Industrial Grade.

Reference : Range Finding Toxicity Tests on Flaked Grade Resorcinol; Industrial Hygiene Foundation of America Inc., Oct-Dec 1962 (conducted by Koppers Company)
Reliability : (2) valid with restrictions
14.09.2005 (103)

Species : rabbit
Concentration : 500 mg
Exposure : No data
Exposure time : 24 hour(s)
Number of animals : 6
Vehicle : physiol.saline
PDII : 4.4
Result : irritating
Classification : irritating
Method : other: Patch-Test
Year : 1976
GLP : no data
Test substance : Other TS:

Test substance : Resorcinol Flake
Reliability : (4) not assignable
14.09.2005 (37)

Species : Rabbit
Concentration : 500 mg
Exposure : Occlusive
Exposure time : 24 hour(s)
Number of animals : 6
Vehicle : physiol. saline
PDII : 2.8
Result : slightly irritating
Classification : irritating
Method : other: FDA Guidelines (Federal Register 38, no.187, 9/27/1973, p. 27019)
Year : 1979
GLP : no data
Test substance : Other TS:

Test substance Nako-Brown 3G
Method : 6 Albino Himalayan rabbits, Hoe: HIMK (SPFWiga) were used in this study. The test substance was Nako-Brown 3G (brownish-gray powder)

The fur was removed from the flank skin of 6 rabbits (weighing 1.5 to 2.5 kg) with an electric razor over an area of at least 6 x 3 cm.' One half of the shorn skin was also scarified with a cupping instrument. 500 mg of the original substance (made into a paste with 0.5 ml of physiologic NaCl solution) is applied to a 2.5 cm^2 gauze pad. The pads were firmly applied to the prepared skin with adhesive tape and then covered with an inert impermeable PVC film (6 - 8 cm wide). Then the rump of the animal was wrapped in an elastic permanent bandage (Elastoplast®). It was left on for 24 hours. The first evaluation of the irritant effect was made immediately upon removal of the bandage; additional evaluations were performed at 48 and 72 hours after

application. Based on the findings, the irritant index was determined according to the classification system described under § 1500.41 in Federal Register 38, No. 187, 9/27/1973, p. 27019.

Results : After application of the paste dye, an irritant index of 2.8 was determined. The flanks of the animals presented with large areas of black dye deposits and a hardened skin (5 out of 6 animals). The dye is therefore evaluated as slightly irritating to the skin.

Reference : Hoechst AG (1979): Skin and Mucosa tolerance of Nako-Brown 3G in rabbits(Report number 172/79)

Reliability : (2) valid with restrictions
No data on purity, no data on GLP

14.09.2005 (52)

5.2.2 EYE IRRITATION

Species : rabbit
Concentration : No data
Dose : .1 g
Exposure time : 72 hour(s)
Comment :
Number of animals : 6 males
Vehicle : None
Result : Irritating
Classification : Irritating
Method : other: see remark
Year : 1962
GLP : No data
Test substance : Other TS:

Test substance : Flaked and Industrial Grade Resorcinol

Method : The study was conducted in accordance with Federal Hazardous Substance Labeling Act (FHSLA), Federal Register Aug 12, 1961, p 7333-7341, Part 191 "Hazardous Substances Definitions and Procedural and Interpretative Regulations, Final Order".

Flaked Grade (deep, ivory colored solid) and Industrial Grade (dark brown-colored solid), no purity data available

Six male albino rabbits were treated in determining the extent of injury that might be expected following accidental contamination of the eyes with each material. Two to four hours prior to the application of the material upon the cornea and into the conjunctival sac, the eyes were stained with fluorescein to assure the use of undamaged eyes. Since the material was water soluble, the standard test procedure was modified to test both the dissolved material and the semi-solid in its usual state. One tenth of a gram of the material was applied to one eye of each of six rabbits, the six untreated eyes serving as controls. The exposed eyes were not washed following application of the material. The eyes were examined and evaluated at 24 hours, 48 hours, and 72 hours after treatment for gross damage to the palpebral and bulbar conjunctivae, to the iris, and to the cornea. All damaged eyes were examined periodically thereafter for a maximum period of two weeks to evaluate the permanence of the damage and the rate and degree of repair.

Result : There was no significant difference in the response of the eyes of rabbits to Flaked or Industrial Resorcinol.
The application of 0. 1 gm. of either of the test materials into the eyes of male, albino rabbits similarly produced severe conjunctivitis, iritis, corneal opacities, and corneal ulcerations. At the conclusion of the 14-day observation period, all of the exposed eyes revealed kerataconus and pannus formation. The test substance, therefore, is an eye irritant as

defined in the regulations pursuant to the FHSLA.

Reference : Range Finding Toxicity Tests on Flaked Grade Resorcinol; Industrial Hygiene Foundation of America Inc., Oct-Dec 1962 (conducted by Koppers Company)

Reliability : (2) valid with restrictions
13.09.2005 (103)

Species : rabbit
Concentration : 100 mg
Dose : .1 ml
Exposure time : 24 hour(s)
Comment : rinsed after (see exposure time)
Number of animals : 6
Vehicle : physiol. saline
Result : highly irritating
Classification : irritating
Method : other: see remark
Year : 1979
GLP : no data
Test substance : Other TS:

Test substance : Nako-Brown 3G
Method : This study was conducted in accordance with FDA guidelines Federal register 38, No. 187 9/27/1973 p 27019. Albino Himalayan rabbits (Hoe: HIMK (SPFWiga), weighing 1.5 to 2.5 kg were used. 100 mg of the original substance presented in the form of brownish-gray powder (made into a paste with 0.1 ml of physiological NaCl solution) was applied to the conjunctival sac of the left eye. The right eye served as an untreated control. The irritant effect was evaluated with a magnifying glass 1, 7, 24, 48 and 72 hours after application. 24 hours after the exposure, the eyes were rinsed with physiological saline solution. The 48 and 72 hour values were recorded after additional instillation of one drop of fluorescein sodium in a dilution of 1:10000 = 0.01%. A numerical evaluation was made according to the classification system indicated in the "Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics", FDA, Austin, Texas, p. 51, 1975.
Results : After application of the paste dye, the highest irritant index was 70 after 48 hours. The nictating and mucous membranes of all rabbits was dark brown (1 - 24 hours postadministration) and gray to black (48 and 72 hours after administration). According to the FDA Guidelines, the test substance is to be evaluated as severely irritating to the mucosa.
Reference : Hoechst AG (1979): Skin and Mucosa tolerance of Nako-Brown 3G in rabbits(Report number 172/79)
Reliability : (2) valid with restrictions
14.09.2005 (52)

Species : guinea pig
Concentration : 2.5 %
Dose : 100 µl
Exposure time : No data
Comment : None
Number of animals : No data
Vehicle : No data
Result : not irritating
Classification : not irritating
Method : other:
Year : 1987
GLP : no data
Test substance : no data

Method : The Draize irritation test was performed on guinea pigs by instilling 100µl of 2.5% solution into the eye. Eye irritation on three distinct tissues (cornea, conjunctiva, iris) were scored after 0.5, 1,2,3,4,6,7 and 24 h.

Remark	:	Instillation of 100 ul of a 2.5% test substance solution (Draize method)
Reference	:	Comparison of in vitro cell toxicity with in vivo eye irritation Bracher et al. (1987): Mol. Technol. 1, 561-570
Reliability	:	(4) not assignable No data on purity, no data on number of animals, no data on GLP

14.09.2005 (11)

5.3 SENSITIZATION

Type	:	Guinea pig maximization test
Species	:	guinea pig
Number of animals	:	10
Vehicle	:	See remark
Result	:	sensitizing
Classification	:	Sensitizing (R43)
Method	:	OECD Guide-line 406 "Skin Sensitization", adopted May 12, 1981; Directive 67/548/EEC, Method B.6
Year	:	1989
GLP	:	yes
Test substance	:	Other TS:

Test substance
Resorcinol, purity 99.9% (white flakes)

Method : Twenty Pirbright White guinea pigs were used to determine the potential for sensitization: treatment group: 10; control group: 5; accompanying group: 20

Vehicles used were 50% Freund's complete adjuvant and 0.9% isotonic saline solution. The Freund's adjuvant was mixed immediately prior to use with an equal volume of 0.9% NaCl solution. This 50% Freund's adjuvant was injected intradermally into the test animals.

For the dermal applications and intradermal injections, resorcinol was diluted with 0.9% NaCl solution. For intradermal injections of the test substance in Freund's adjuvant, resorcinol was diluted with 0.9% NaCl solution and this dilution was then mixed with an equal volume of the original Freund's adjuvant.

The intradermal induction exposure was conducted with 2% test substance in 0.9% NaCl solution; dermal induction exposure and the dermal challenge exposure with 25% test substance in 0.9% NaCl solution.

Exposure Groups:

Position	Volume Applied (ml)	Conc. %	Substance vehicle
1	2 x 0.1	-	50% Freund's adjuvant
2	2 x 0.1	2.0	0.9% Nacl solution
3	2 x 0.1	2.0	50% Freund's adjuvant

Control and Accompanying groups received only the vehicle without the test substance.

0.5 ml of the test substance preparation or the vehicle was applied to a 2 x 4 cm cellulose pad during the dermal induction exposure which was conducted on Day 8. The pad covered the area of the intradermal injection sites. An occlusive bandage with impermeable film and elastic binding sealed the application site for 48 hours. The exposure group received 25.0% test substance in 0.9% NaCl solution. Control and accompanying group received only 0.9% NaCl solution.

On Day 10 the occlusive bandage was removed, any irritating effect was recorded. The test animal were observed up to Day 21.

On Day 22 dermal challenge exposure was performed. The fur was removed mechanically from a 5 x 5 cm area on the left flank of the test animals. 0.5 ml of the test substance preparation was applied to a 2 x 2 cm cellulose pad. An occlusive bandage with impermeable film and elastic adhesive binding sealed the application site for 24 hours. Exposure and control Group (left flank) received 25.0% test substance in 0.9% NaCl solution.
On Day 23 the occlusive bandage was removed. Day 24 and 25, evaluation of the skin was conducted.
The repeat dermal challenge exposure was conducted on Day 29. Exposure and control group (right flank) were exposed to 25.0% test substance in 0.9%Nacl solution.

Results : The exposed animals showed no signs of intoxication throughout the entire test period.

The intradermal injections with Freund's adjuvant (with and without test substance) led to a clear reddening and swelling of the injection sites. As of Day 3 post-administration, the injection sites were also hardened. Five days post-administration, scabbing was also observed. The injection sites treated with the test substance in 50% Freund's adjuvant were also brown-colored on Days 1 and 2 after administration; after 5 days post-administration, partial necrosis was observed. After intradermal injection of the test substance in 0.9% NaCl solution, minor reddening and swelling appeared on Days 1 and 2. After removal of the occlusive bandage on Day 10, the application sites exposed to Freund's adjuvant were reddened, swollen and hardened in animals in the control, accompanying and exposure groups. Necrosis and in part, open wounds, appeared as well. No signs of irritation were observed at the application sites in Position 2 (without Freund's adjuvant). The trend in body weight of the exposed animals was not impaired. After the first challenge exposure, very slight to clearly circumscribed erythema was observed on the skin of two or three animals in the exposure group 24 and 48 hours after removal of the occlusive bandage. The skin of the control animals was clear of signs of irritation. After the second challenge exposure, very slight to clearly circumscribed erythema was observed on the skin of 7 animals in the exposure group 24 hours and on 5 animals in the exposure group 48 hours after removal of the occlusive bandage. Minor swelling was also observed in one animal in the exposure group 24 hours after removal of the occlusive bandage. The skin of the control animals was clear of signs of irritation.
Seven animals in the exposure group presented with a positive reaction after the challenge exposure. The relative frequency of the positively reacting animals is thus over the limit value of 30%. Therefore, the test substance is designated as sensitising.

Reference : Hoechst AG (1989): Study of Sensitizing Properties in Pirbright Wite Guinea Pigs on the Maximization Test (89.0483)

Reliability : (1) valid without restriction
14.09.2005 (54)

5.4 REPEATED DOSE TOXICITY

Type	:	Sub-acute
Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	gavage
Exposure period	:	2 weeks
Frequency of treatm.	:	Once daily for 5 days a week (12 doses dispensed over 17 days)
Post exposure period	:	None
Doses	:	0, 27.5, 55, 110, 225, 450 mg/kg/bw
Control group	:	yes
NOEL	:	450 mg/kg bw

Method	:	Other: see remark
Year	:	1991
GLP	:	No data
Test substance	:	Other TS: see remark
Test substance	:	Obtained from NAPP Chemicals, Incorporated. Preparation in water, purity >99%. Resorcinol USP grade. Lot number IN-79-7087
Method	:	Groups of five rats of each sex, aged 6 to 7 weeks, were administered 0, 27.5, 55, 110, 225 or 450 mg/kg resorcinol in deionised water by gavage. All doses were given once daily for 5 days per week so that 12 doses were dispensed over 17 days. The animals were observed for mortality and for clinical signs related to chemical administration. Body weights were recorded at study initiation, weekly and at study termination. A necropsy was performed on all animals. Organ weights were recorded for brain, heart, right kidney, liver, lungs and thymus for all animals. Tissues were fixed in 10% neutral buffered formalin and processed for micrscopic examination. Histopathologic examinations were conducted on the brain, heart, kidney, liver, lung and thymus of rats receiving 450 mg/kg. Clinical pathology was not performed. Statistical analyses were performed using Williams' or Dunnett's test.
Result	:	All rats survived to the end of the study. Body weight development lay in same range as that of control. Clinical signs of toxicity appeared within half an hour of dosing and lasted 1 to 2 hours. Hyperexcitability and tachypnea were observed in males receiving 225 to 450 mg/kg. Females receiving doses of 55 mg/kg and greater showed hyperexcitability and those receiving 110 and 450 mg/kg showed tachypnea. High dose females had signifiacntly decreased absolute and relative thymus weights. There were no substance-related macroscopic or histopathological changes.
Reference	:	NTP Technical Report on the Toxicology and Carcinogenesis Studies of Resorcinol (CAS No. 108-46-3) in F344/N Rats and B6C3F$_1$ Mice (Gavage Studies) NIH Publication No. 91-2858
Reliability 14.09.2005	:	(1) valid without restriction (1)
Type	:	Sub-chronic
Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	gavage
Exposure period	:	13 weeks
Frequency of treatm.	:	Once a day 5 days a week
Post exposure period	:	
Doses	:	0, 32, 65, 130, 260, 520 mg/kg/bw
Control group	:	yes
NOEL	:	260
Method	:	Other: see remark
Year	:	1991
GLP	:	no data
Test substance	:	Other TS: see remark
Test substance	:	Obtained from NAPP Chemicals, Incorporated. Preparation in water, purity >99%. Resorcinol USP grade. Lot No. IN-79-7087
Method	:	Rats were observed for 14 to 16 days before dosing and were 6 to 7 weeks at start of study. Groups of 10 rats of each sex were administered 0, 32, 65, 130, 260 or 520 mg/kg of resorcinol in deionised water by gavage. Animals were observed twice daily for mortality and weekly for clinical signs of toxicity throughout the study. Body weights were recorded at study initiation, weekly and at study termination.

At study termination blood samples were collected from the orbital sinus of each surviving animal for measurement of:
Hematology: hematocrit, hemoglobin, erythrocytes, mean cell volume, mean cell hemoglobin, concentration leukocytes, segmented neutrophils, lymphocytes, monocytes and eosinophils.
Clinical chemistry: urea, nitrogen, creatinine, sodium, potassium, chloride, calcium, phosphorus, total protein, albumin, ag/gl ratio, total biliribin, methemoglobin, alanine aminotransferase, aspartate aminotransferase, sorbitol dehydrogenase, cholinesterase, triiodothyronine and thyroxine.
A gross necropsy was performed on all surviving animals. A complete histopathological examination was performed on all control animals and animals dosed at 260 or 520 mg/kg bw and all animals that died during the study. Tissues examined were: adrenal glands, aorta, bone, brain, clitoral gland, esophagus, heart, kidneys, large intestine, liver, lungs, mammary gland, mandibular lymph node, mesenteric lymph node, nasal cavity, ovaries, pancreas, parathyroids, pituitary, preputial gland, prostrate, salivary gland, skin, small intestine, spleen, stomach, testes, thymus, thyroids trachea, urinary bladder and uterus.

Organ weights were recorded for adrenal gland, brain, heart, right kidney, liver, lung and thymus for all animals and the right testis for all males.
A complete histopathological examination was conducted on all control animals and animals receiving 260 or 520 mg/kg and all animals that died during study.

Result : All female rats and all but 2 males receiving 520 mg/kg died from compound related toxicity during first 4 weeks of the study. On day 2 rats receiving 260 mg/kg were given 520 mg/kg in error. Within 5 days 2 males and 5 females died from this group. These deaths were attributed to error in dosing since no further deaths occurred from rats receiving this dose.

The final body weight and changes in mean body weight weight of rats were similar to that of controls. Tremors were observed in high-dose rats of both sexes. Males receiving 130 or 260 mg/kg and females receiving 65, 130 or 260 mg/kg had significantly increased absolute and relative liver weights. Absolute and relative adrenal gland weights were significantly increased in all surviving male dosed groups.

No biologically significant differences in hematology or clinical chemistry were observed. A few significant differences in various parameters scattered among the groups were seen, but none were considered biologically significant. There were no gross or microscopic lesions attributable to treatment.

Reference : NTP Technical Report on the Toxicology and Carcinogenesis Studies of Resorcinol (CAS No. 108-46-3) in F344/N Rats and B6C3F_1 Mice (Gavage Studies) NIH Publication No. 91-2858

Reliability : (1) valid without restriction
14.09.2005 (1)

Type : Sub-acute
Species : mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : gavage
Exposure period : 2 weeks
Frequency of treatm. : Once a day 5 days a week (12 doses over 17 days)
Post exposure period : none
Doses : 0, 37.5, 75, 150, 300, 600 mg/kg/bw
Control group : yes
NOEL : 100 mg/kg bw
Method : Other: see remark
Year : 1991

GLP	:	No data
Test substance	:	Other TS: see remark
Method	:	Groups of five mice of each sex aged 7 to 8 weeks were administered 0, 37.5, 75, 150, 300 or 600 mg/kg resorcinol in deionised water by gavage. All doses were given once daily for 5 days per week so that 12 doses were dispensed over 17 days. The animals were observed for motality and for clinical signs related to chemical administration. Body weights were recorded at study initiation, weekly and at study termination. A necropsy was performed on all animals. Organ weights were recorded for brain, heart, right kidney, liver, lungs and thymus for all animals. Tissues were fixed in 10% neutral buffered formalin and processed for micrscopic examination. Histopathologic examinations were conducted on the brain, heart, kidney, liver, lung and thymus of mice receiving 300 and 600 mg/kg. Clinical pathology was not performed. Statistical analysis was performed using Williams' or Dunnett's test.
Result	:	Body weight development lay in same range as that of control; in the 600 mg/kg body weight dose group, 4 out of 5 males and 5 out of 5 females died; in the 300 mg/kg body weight group, 1 out of 5 males died. The death of a control male was due to a gavage accident. Clinical findings, including prostration and tremors, were recorded among males receiving 150 mg/kg and greater and females receiving 300 mg/kg or greater. these findings usually appeared within an hour of dosing and lasted 1 to 2 hours. No biologically significant changes in organ weight were observed. No substance related macroscopic or histopathological changes.
Test substance	:	Obtained from NAPP Chemicals, Incorporated. Preparation in water, purity >99%. Resorcinol USP grade. Lot No. IN-79-7087
Reference	:	NTP Technical Report on the Toxicology and Carcinogenesis Studies of Resorcinol (CAS No. 108-46-3) in F344/N Rats and B6C3F$_1$ Mice (Gavage Studies) NIH Publication No. 91-2858
Reliability 13.09.2005	:	(1) valid without restriction (1)

Type	:	Sub-chronic
Species	:	mouse
Sex	:	male/female
Strain	:	B6C3F1
Route of admin.	:	gavage
Exposure period	:	13 weeks
Frequency of treatm.	:	Once a day, 5 days a week
Post exposure period	:	
Doses	:	0, 28, 56, 112, 225, 420 mg/kg/bw
Control group	:	Yes
NOEL	:	225 mg/kg bw

Test substance	:	Obtained from NAPP Chemicals, Incorporated. Preparation in water, purity >99%. Resorcinol USP grade. Lot No. IN-79-7087
Method	:	Mice were observed for 14 to 16 days before dosing and were 6 to 7 weeks at start of study. Groups of 10 mice of each sex were administered 0, 28, 56, 112, 225 or 420 mg/kg of resorcinol in deionised water by gavage. Animals were observed twice daily for mortality and weekly for clinical signs of toxicity throughout the study. Body weights were recorded at study initiation, weekly and at study termination. At study termination, blood samples were collected from the orbital sinus of each surviving animal for measurement of: Hematology: hematocrit, hemoglobin, erythrocytes, mean cell volume, mean cell hemoglobin, concentration leukocytes, segmented neutrophils, lymphocytes, monocytes and eosinophils.

Clinical chemistry: urea, nitrogen, creatinine, sodium, potassium, chloride, calcium, phosphorus, total protein, albumin, ag/gl ratio, total bilirubin, methemoglobin, alanine aminotransferase, aspartate aminotransferase, sorbitol dehydrogenase, cholinesterase, triiodothyronine and thyroxine.
A gross necropsy was performed on all surviving animals.
Organ weights were recorded for adrenal gland, brain, heart, right kidney, liver, lung and thymus for all animals and the right testis for all males. A complete histopathological examination was performed on all control animals and animals dosed at 225 or 420 mg/kg bw and all animals that died during the study. Tissues examined were: adrenal glands, aorta, bone, brain, clitoral gland, esophagus, heart, kidneys, large intestine, liver, lungs, mammary gland, mandibular lymph node, mesenteric lymph node, nasal cavity, ovaries, pancreas, parathyroids, pituitary, preputial gland, prostate, salivary gland, skin, small intestine, spleen, stomach, testes, thymus, thyroids trachea, urinary bladder and uterus.

Result : Eight mice of each sex receiving 420 mg/kg died by week 4 of the studies from compound-related toxicity. All except two of these deaths occurred during the first week. The death of one male receiving 112 mg/kg was due to improper gavage. The final mean body weight of the two surviving high-dose male mice was significantly less than controls. The final mean body weights and in mean body weight of mice receiving resorcinol were similar to those of the controls. Clinical signs of toxicity recorded for the high-dose animals included dyspnea, prostration, and tremors. Clinical signs generally appeared within one-half hour of dosing.

Significant decreases were noted in absolute and relative adrenal gland weights for males receiving 28, 112 and 225 mg/kg. A few other differences in various organ weights were scattered among the study groups, but none were considered biologically significant.

Reference : NTP Technical Report on the Toxicology and Carcinogenesis Studies of Resorcinol (CAS No. 108-46-3) in F344/N Rats and B6C3F$_1$ Mice (Gavage Studies) NIH Publication No. 91-2858

Reliability : (1) valid without restriction
14.09.2005 (1)

Type : Sub-chronic
Species : Rabbit
Sex : Male/female
Strain : New Zealand White
Route of admin. : Percutaneous
Exposure period : 13 weeks
Frequency of treatm. : Twice weekly for 13 weeks
Post exposure period : none
Doses : 1 ml/kg
Control group : Yes
NOEL : 1 ml/kg
Method : Other: see remarks
Year : 1976
GLP : No data
Test substance : Other TS: see remark

Test substance 12 hair dye formulations containing Resorcinol
Method : The 12 hair dye formulations were applied topically twice weekly for 13 wk to groups of 12 adult New Zealand white rabbits (six of each sex). The formulation was mixed with an equal volume of 6% hydrogen peroxide prior to application. The sites of application on the dorsolateral aspects of the thoracic-lumbar area (one on each side of the midline) were alternated to minimize skin irritation. The dose was 1 ml/kg of the 1 :1 oxidation mixtures and of those formulations used as is. This was the maximum dose that could be applied on the side of the rabbits without runoff. The hair at the site of application on the back and

sides of each rabbit was clipped short throughout the study. The application sites on three animals of each sex in each group were abraded on the first treatment day of each week. The rabbits were restrained in holding stocks for 1 hr following each application and were then shampooed, rinsed, dried, and returned to their cages.
The rabbits in the three independent control groups of 12 rabbits each were treated identically except that no dyes were applied. The animals were weighed weekly during the study. Hematologic and clinical chemistry determinations and examination of urine was performed on all animals at 0, 3, 7, and 13 wk. These studies included determination of complete blood count, methamoglobin, fasting blood sugar, blood urea nitrogen, alkaline phosphatase, and serum glutamic oxaloacetic transaminase. Urine was examined for color, pH, albumin, glucose, occult blood and micrscopic elements.
The clinical chemistry determinations were performed on blood obtained by cardiac puncture by SMA-12 analysis using the Technicon auto analyser. Hematoglogy studies utilised the automated electronic Coluter F counter and reference methods (Schalm, 1975) Ames Labstix were used for the urinalysis.
All survivors were sacrificed after 13 wk and examined for gross abnormalities. Organ-body weight ratios were determined for liver, kidneys, adrenals, heart, thyroid, spleen, and brain. Twenty-five tissues [skin from treated and untreated areas, lymph nodes (mesanteric, axillary, and cervical), spleen, stomach, duodenum, colon, liver, gall bladder, adrenals, nerve with adjacent muscle, eyes, pancreas, kidneys, urinary bladder, ovaries, testes, bone, bone marrow, heart, lung, thyroid, brain, and skeletal muscle under the site of application and elsewhere (thigh)] from each animal were stained with hematoxylin and eosin and examined microscopically. Statistical analysis of the data on body weight gains, hematology, clinical chemistries, and absolute and relative organ weights was performed using the analysis of variance F test and Student's t test. When variances differed significantly, Student's *t* test was modified (t') and Cochran's approximation was utilized (Snedecor and Cochran, 1967).

Result : No evidence of compound-induced toxicity was seen. Body weight gain of all test groups was at least equal to that of the controls. Five control and five test animals died during the study due to complications resulting from cardiac puncture while collecting blood. There were scattered statistically significant differences in the clinical chemistry and hematologic values between test and control groups at the various sampling intervals. However, these differences were not considered to be of toxicologic significance because of either the direction or continuity of the differences or the fact that they fell within the range of historical control values.
There were a few instances when there were statistically significant differences in relative organ weights between a test group and the combined controls where the differences were not significant when the group was compared with each control group separately. In no instance were any of these differences accompanied by histomorphologic evidence of toxicity. The results of the urinalyses were unremarkable. No dye discoloration of the urine was seen at any time during the test. The treated skin showed slight thickening in some groups, particularly groups 7403 and P-21. This was not unexpected, due to the frequency of dye application

Reference : Burnett et al. Journal of Toxicology and Environmental Health, 1:1027-1040, 1976

Reliability : (2) valid with restrictions
14.09.2005

(15)

Type : Sub-acute
Species : Rat and guinea pig

Sex	:	no data
Strain	:	no data
Route of admin.	:	inhalation
Exposure period	:	2 weeks
Frequency of treatm.	:	6 hour per day
Post exposure period	:	several months
Doses	:	See remark
Control group	:	yes
Method	:	other
Year	:	1976
GLP	:	No data
Test substance	:	Other TS:

Test substance Resorcinol, Flake Grade

Method : The experiments were designed to determine any damage to the lungs and trachea or evidence of an allergic reaction in the respiratory tract.
Two types of studies were made: throat spray tests and inhalation studies
Throat spray tests
In these tests, groups of guinea pigs and rats received three daily throat sprayings with a 1% water solution of resorcinol for a period of two weeks. They were maintained and examined weekly for ten additional weeks. A control group was sprayed with water only.

Inhalation tests
Rats rabbits and guinea pigs were exposed to resorcinol at a concentration of 34 mg/M^3, six hours daily for a period of two weeks, then maintained for several months, with periodic sacrifices.

Result : Throat Spray test
The animals demonstrated no gross evidence of respiratory damage. Histopathological examination of the lungs showed several animals with tracheo-bronchitis, but the incidence was no different that that of the control group. During the two weeks of actual spraying the throats of the animals appeared to be irritated, but this condition cleared up after exposure was terminated.

Inhalation test
No evidence of toxic effects was noted.

Reference : The benzenediols: catechol, resorcinol and hydroquinone – a review of the industrial toxicology and current industrial exposure limits
C.W. Flickinger, Manager, Industrial Hygiene & Safety Group, Koppers Company Inc., Research Department, Monroeville, Pennsylvania 15146, USA, Am. Ind. Hyg. Assoc. J. 37, 596-606

Reliability : (2) valid with restrictions
14.09.2005 (37)

Type	:	Sub-acute
Species	:	rat
Sex	:	no data
Strain	:	No data
Route of admin.	:	oral feed
Exposure period	:	2 weeks
Frequency of treatm.	:	No data
Post exposure period	:	Several months
Doses	:	5% (approx. 2500 mg/kg bw)
Control group	:	no data specified

Result : Increased thyroid gland weight; reduced T4 content in plasma; lower half-life time for T4.

Reliability : (4) not assignable
14.09.2005 (6)

Type	:	Sub-acute
Species	:	rat
Sex	:	male
Strain	:	No data
Route of admin.	:	oral feed
Exposure period	:	4 weeks
Frequency of treatm.	:	No data
Post exposure period	:	No data
Doses	:	0-260 mg/kg bw
Control group	:	yes
Result	:	No mortality and no clinical symptoms, no hispathological findings, no influence on body weight development, decrease in relative weight of adrenal gland in all treated animals.
Reliability	:	(4) not assignable

14.09.2005 (36)

Type	:	Sub-acute
Species	:	rat
Sex	:	male
Strain	:	No data
Route of admin.	:	oral feed
Exposure period	:	8 weeks
Frequency of treatm.	:	No data
Post exposure period	:	No data
Doses	:	0.8% (approx. 800 mg/kg body weight/day for an assumed feed consumption of 100 g/kg body weight/day)
Control group	:	yes
Result	:	Body weight development, feed and water consumption lay in the range of those of the control; no substance-related changes in the mucous membrane of the fore stomach or glandular stomach.
Reliability	:	(4) not assignable

14.09.2005 (112)

Type	:	Sub-chronic
Species	:	rat
Sex	:	male/female
Strain	:	Wistar
Route of admin.	:	inhalation
Exposure period	:	90 days
Frequency of treatm.	:	8 hours
Post exposure period	:	No data
Doses	:	No data
Control group	:	No data
Method	:	other: not concluded to any guidelines
Year	:	1977
GLP	:	No data
Test substance	:	Other TS:
Test substance	:	Resorcinol Lot 5824-3, deep, ivory-colored solid in a relatively large particulate state
Remark	:	Number of animals: 50
Method		The Resorcinol was dissolved in distilled water prior to initiation of each exposure. This solution was dispersed into a 4.5' x 4.0' x 2.0' chamber, having a gasketed, removable plexiglass front, by means of a De Vilbiss Ultrasonic Nebulizer. The average concentration was 213 ppm. Ten minute samples at 2 liters per minute were taken every two hours using 2 midget impingers in series, each containing 10 ml of 0.1 N HCl. These were analyzed by UV spectroscopy at 273.5 millimicrons with a 100 millimeter cell.

Twenty-five males and twenty five females of the Hilltop Lab Animals, Inc. HLA-SD Strain were obtained for the study. All of the rats tested had a laboratory history of normal growth rate and good appearance and behavior. The animals were housed, as well as exposed, in wire cages. They were fed ground Purina Laboratory Chow and received tap water from bottles attached to the front of the cage. All animals were weighed daily and their food consumption monitored. A non-exposed control group of rats, five males and five females, were deprived of food and water for an eight-hour period per day to correspond with the exposure period of the test animals. Another group of control animals, five males and five females, were given a measured allotment of food based upon the average food consumption of the test animals. A comparison of the resultant growth curves was the measure of effect. The purpose of this supplemental group was to determine whether a retarded growth rate became evident in the test group, it could be due to a decrease in diet consumption.

Prior to initiation of the exposure, a 10 ml aliquot of blood for physiological and chemical analysis was drawn by means of cardiac puncture from each of sixteen rats. These determinations served as a base line for comparison after the 90 day exposure was completed. At the same time urine samples were collected from a group of nine animals.

Result : Because of what appeared to be excessively high mortality (20% in the male group and 28% in the female group), the exposure was temporarily terminated at the request of the sponsor after 64 exposures. One half of the survivors of each group were sacrificed one week later and blood and urine samples collected from a representative number.

After a two week pasture period, the remaining exposed animals appeared to have recovered sufficiently as indicated by their growth rate so that exposures were again initiated until a total of 90 exposures were completed.

Growth rates of both the Resorcinol and the pair-fed control groups were significantly affected. Basically this was the result of diet intake. Statistical evaluation of weekly diet consumption showed significant differences ($p < 0.001$) in both male and female groups when laboratory controls were compared with the Resorcinol exposed group. In comparing the diet consumption of the pair-fed controls with the Resorcinol animals no significant difference was apparent in either the males ($p = 0.69$) or the females ($p = 0.21$).

Significant differences between laboratory controls and Resorcinol rats were also seen in the male liver, kidney and spleen weights and in the female kidney, adrenal and spleen weights. Both lung and heart weights of the Resorcinol group were significantly different from the pair-fed controls, as were the female spleen weights.

In comparing male laboratory controls with male pair-fed controls, significant differences were found in body, liver, kidney, lung, heart and spleen weights. Among the female controls, the pair-fed group differed significantly in body, lung, heart and adrenal weights from the laboratory controls.

Upon histopathological examination, 5 of the 12 rats that died prior to completion of the exposures, showed infections resulting in acute exudative inflammations demonstrable in the heart, lungs and liver. In other 7 animals, the causes of death could not be determined from the sections at hand.

Because no significant qualitative or quantitative differences were noted in rats after 64 exposures to resorcinol as compared to lesions in rats after 90 exposures, one description will encompass all lesions in exposed rats.

The most important changes were seen in the thyroid glands of the exposed animals. These glands were hyperplastic. The hyperplasia affected 39% of the rats (15 of 38). It was characterized by a great increase in the number of acini. These were small, lined by columnar epithelium enclosing a very small lumen. The acini contained little or no colloid. The thyroid glands of the control rats were not hyperplastic. Although these obtained some small acini, there were many larger ones lined by cuboidal cells. The larger acini were filled with colloid.

It is noteworthy that the lungs gave no indication of significant disease. One to three alveolar giant cells without associated changes were found in three exposed rats and one laboratory control. No foreign material was observed within the giant cells. An occasional small cluster of macrophages, containing no visible foreign material was found in one surviving exposed rat and one control. These were not associated with other structural changes.

The most commonly observed abnormality was the presence of minimal lymphocytic infiltration in a few widely scattered portal zones of livers in about 50% of the exposed rats and 35% of the controls. There were also incidental findings that are believed to be unrelated to the exposure. These include acute hepatitis, acute myocarditis, focal myocardial fibrosis, interstitial pneumonitis, splenic hemosiderosis, hydronephrosis, and minimal focal lymphocytic infiltration of renal tissue.

Inasmuch as 39% of the rats exposed to Resorcinol developed hyperplasia of the thyroid gland and none of the control animals manifested this lesion, the conclusion appears well founded that there was systemic absorption of Resorcinol and that this affected the thyroid gland.

No pulmonary changes can be ascribed to the inhalation of Resorcinol. Although several alveolar giant cells and macrophage clusters were noted in a few exposed animals, similar findings were also present in control rats.

Since minimal portal lymphocytic infiltration occurred in both exposed and control animals, this does not appear to be causally related to the Resorcinol exposure. All other pathological findings appear to be also incidental lesions unrelated to the experimental exposure.

At the conclusion of the 90 day exposure period, blood was drawn from 17 Resorcinol rats and 12 controls for physiological and chemical analysis. There were significant differences in glucose values before and after exposure in both males and females. However, this was also true in the values obtained before exposure and in those of the controls (sampled 5 ¾ months after initiation of exposure). Only the female group showed significantly different BUN and SGPT values before and after exposure. Again, these same differences occurred in the control group. The alkaline phosphatase values of exposed rats were not significantly different from those of the control group.

Hematocrit and lymphocyte values before and after exposure differed significantly in both the males and females. The lymphocyte values of the male control group sampled 5 ¾ months after the start of exposure was significantly different from that of the male group before exposure. Significant differences were found in the hematocrit values before and after

exposure in both males and females. There are significant increases in hematocrit values, in both males and females after exposure when compared with the control values.

In comparing the red blood cell values before and after exposure, the females showed a significant increase. This same significance exists in a comparison of the controls with the exposure group. The red blood cells of the male control group also differed significantly from the before exposure group.

No significant differences were found in comparing white blood cell counts of the control group with those of the post exposure test animals, but in the male animals there was a significant difference between before and after exposure.
Urine samples were collected on ten test animals and eight controls after 90 days exposure. Generally, no differences were evident between before and after exposure. Six of the nine urine samples collected before exposure showed a negative albumin. The remaining three pre-exposure samples and all samples taken after exposure, as well as those from controls, were positive.

Conclusion : Exposure of 25 male and 25 female albino rats to 213 ppm Resorcinol as an atomized mist for 8 hours per day for 60 days (over 4 months) or 90 days (over 5 3/4 months) resulted in significant effects on growth rate and on some of the organ weights. No significant pathological abnormalities were found which might account for these differences. Hyperplasia of the thyroid gland was observed in more than one-third of the animals, but this finding was not accompanied by any significant differences in the thyroid weight values. A supplemental group of pair-fed controls provided data that appears to substantiate the probability that the effect on growth of the exposed rats was primarily due to the decrease in diet consumption.

Resorcinol exposure appears to result in a mild albuminuria and increased specific gravity of the urine. That this may be due at least in part to the decreased consumption of food and water is suggested by the absence of specific pathology in the kidneys. Bacteria and pus cells were also increased in the urine after exposure. Although some significant differences were observed in blood chemistry and hematology values, no valid conclusion can be drawn from them.

Reference : Final Report on 90 day Inhalation-Thyroid Exposure to Resorcinol; Industrial Health Foundation Inc. Feb 1977 American Industrial Hygiene Assoc. 37, Oct. 1976 (conducted for Koppers Company)

Reliability : (2) valid with restrictions
14.09.2005 (33)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Ames test
System of testing	:	Salmonella typhimrium TA98, TA100, TA1535, TA1537
Test concentration	:	0, 33, 100, 333, 1000, 3333 µg/plate
Cycotoxic concentr.	:	N/A
Metabolic activation	:	with and without
Result	:	negative
Method	:	other:Haworth et al. (1983)
Year	:	1991
GLP	:	no data
Test substance	:	Other TS: see remark

Method : Each trial consisted of triplicate plates of concurrent positive and negative controls and of at least five doses of resorcinol. Study was conducted in the presence and absence of exogenous metabolic activation (S-9 mix)

High dose was limited by toxicity or solubility, but did not exceed 10mg/plate.
All assays were repeated

Result : In the assay, a positive response is defined as a reproducible, dose related increase in histidine-independent (revertant) colonies in any one strain/activation combination.

Resorcinol at doses from 33 to 3,333 µg/plate did not induce gene mutations in any of the four strains of Salmonella typhimurium when tested with a preincubation protocol in the presence and absence of Aroclor 1254-induced male Sprague-Dawley rat or Syrian hamster liver S9.

Test substance : Resorcinol sent as a coded aliquot from Radian Corporation (Austin, TX)
Reference NTP Technical Report on the Toxicology and Carcinogenesis Studies of Resorcinol (CAS No. 108-46-3) in F344/N Rats and B6C3F$_1$ Mice (Gavage Studies) NIH Publication No. 91-2858

Reliability : (1) valid without restriction
14.09.2005 (1)

Type : Cytogenetic assay
System of testing : Ovarian cells of the Chinese hamster (CHO)
Test concentration : 750, 1000, 1500 and 2000 µg/ml in the absence of S9 mix and 4000, 4500 and 5000 in the presence of S9 mix
Cycotoxic concentr. : No data
Metabolic activation : with and without
Result : positive
Method : other: Galloway et al (1985, 1987)
Year : 1991
GLP : no data
Test substance : Other TS: see remark

Test substance : Resorcinol sent as a coded aliquot from Radian Corporation (Austin, TX)
Method : In the test without S9, cells were incubated in McCoy's 5A medium with the study chemical for 21 hours; Colcemid was added and incubation continued for 2 to 3 hours. The cells were then harvested by mitotic shake-off, fixed, and stained with Giemsa. For the test with S9, cells were treated with the study chemical and S9 for 2 hours, after which the treatment medium was removed and the cells incubated for 21.8 hours in fresh medium, with Colcemid present for the final 2 hours. Cells were harvested in the same manner as for the treatment without S9.

Cells were selected for scoring on the basis of good morphology and completeness of karyotype (21 ± 2 chromosomes). All slides were scored blind and those from a single test were read by the same person. 100 first-division metaphase cells were scored at each dose level. Classes of aberrations included simple (breaks and terminal deletions), complex (rearrangements and translocations), and other (pulverized cells, despiralized chromosomes, and cells containing 10 or more aberrations).

Remark : Statistical analyses were conducted on both the slopes of the dose response curves and the individual dose points.
Data presented as a percentage of the cells with aberrations. Both the dose response curve and individual dose points were statistically analyzed. A statistically significant ($P<0.05$) difference for one dose point was considered weak evidence for a positive response (+w); significant differences for two or more doses indicated the trial was positive (+) (Galloway et al., 1987).

Result : Resorcinol induced chromosome aberrations without S-9, the response was equivocal with a significant increase in aberrations only at 1000 µg/ml. With S-9 a signifiacnt increase in aberrations was observed at all three doses (4,00, 4,500 and 5000 µg/ml).

Reference : NTP Technical Report on the Toxicology and Carcinogenesis Studies of Resorcinol (CAS No. 108-46-3) in F344/N Rats and B6C3F$_1$ Mice (Gavage Studies) NIH Publication No. 91-2858

Reliability : (1) valid without restriction
14.09.2005 (1)

Type : Mouse lymphoma assay
System of testing : L 5178Y TK +/-
Test concentration : 156.25, 312.5, 625, 1250, 2500, 5000 µg/ml
Cycotoxic concentr. : 5000
Metabolic activation : without
Result : positive
Method : other: McGregor et al (1988a) and Clive et al (1979)
Year : 1991
GLP : no data
Test substance : Other TS: see remark

Test substance : Resorcinol sent as a coded aliquot from Radian Corporation (Austin, TX)
Method : The highest dose of the study compound was determined by solubility or toxicity, and did not exceed 5 mg/mL. Mouse lymphoma L5178Y cells were maintained at 37° C as suspension cultures in Fischer's medium supplemented with 2 mM 1-glutamine, 110 µg/mL sodium pyruvate, 0.05% pluronic F68, antibiotics, and heat-inactivated horse serum; normal cycling time was about 10 hours. To reduce the number of spontaneously occurring trifluorothymidine (TFT) resistant cells, subcultures were exposed once to medium containing THMG (thymidine, hypoxanthine, methotrexate, glycine) for one day, to THG for one day, and to normal medium for 3 to 5 days. For cloning, horse serum content was increased and Noble agar was added.

All treatment levels within an experiment, including concurrent positive and solvent controls, were replicated. Treated cultures contained 6 x 10+6 cells in a 10 mL volume of medium. This volume included the S9 fraction in those experiments performed with metabolic activation. Incubation with study chemical continued for 4 hours, at which time the medium plus chemical was removed and the cells were resuspended in 20 ml of fresh medium and incubated for an additional 2 days to express the mutant phenotype. Cell density was monitored so that log phase growth was maintained. After the 48 hour expression period, 3 x 10+6 cells were plated in medium and soft agar supplemented with TFT for selection of TFT-resistant cells (TK), and 600 cells were plated in nonselective medium and soft agar to determine cloning efficiency. Plates were incubated at 37° C in 5% CO_2, for 10 to 12 days. All data were evaluated statistically for both trend and peak response. Both responses had to be significant ($P<0.05$) for a chemical to be considered capable of inducing TFT-resistance; a single significant response led to a "questionable" conclusion, and the absence of both a trend and a peak response resulted in a "negative" call. Minimum criteria for accepting an experiment as valid and a detailed description of the statistical analysis and data evaluation are presented in Myhr et al (1985).
Result : Resorcinol gave a positive response in the absence of S9 at concentrations ranging from 156.25 to 2,500 µg/ml.; it was not tested with S9.
Reference : NTP Technical Report on the Toxicology and Carcinogenesis Studies of Resorcinol (CAS No. 108-46-3) in F344/N Rats and B6C3F_1 Mice (Gavage Studies) NIH Publication No. 91-2858

Reliability : (1) valid without restriction
14.09.2005 (1)

Type : Sister chromatid exchange assay
System of testing : Ovarian cells of the Chinese hamster (CHO)
Test concentration : 50, 167, 500 and 1670 µg/ml in the absence of S9 mix and 500, 1670 and 5000 in the presence of S9 mix.
Cycotoxic concentr. : 1670 µg/ml in the absence of S9 mix
Metabolic activation : with and without
Result : positive

Method	:	other: Galloway et al (1985, 1987)
Year	:	1991
GLP	:	no data
Test substance	:	Other TS: see remark
Test substance	:	Resorcinol sent as a coded aliquot from Radian Corporation (Austin, TX)
Method	:	CHO cells were incubated for 26 hours with the study chemical in McCoy's 5A medium supplemented with 10% fetal bovine serum, 1-glutamine (2 mM), and antibiotics. Bromodeoxyuridine (BrdU) was added 2 hours after culture initiation. After 26 hours, the medium containing the test chemical was removed and replaced with fresh medium plus BrdU and Colcemid, and incubation was continued for 2 hours. Cells were then harvested by mitotic shake-off, fixed, and stained with Hoechst 33258 and Giemsa. In the SCE test with S9 (metabolic activation), cells were incubated with the chemical, serum-free medium, and S9 for 2 hours. The medium was then removed and replaced with medium containing BrdU and no test chemical and incubation proceeded for an additional 26 hours, with Colcemid present for the final 2 hours. Harvesting and staining was the same as for cells treated without S9. If significant chemical-induced cell cycle delay was seen, incubation time was lengthened to ensure a sufficient number of scorable cells. 50 second-division metaphase cells were scored for frequency of SCE per cell from each dose level. Statistical analyses were conducted on both the slopes of the dose-response curves and the individual dose points. An SCE frequency 20% above the concurrent solvent control value was chosen as a statistically conservative positive response. The probability of this level of difference occurring by chance at one dose point is less than 0.01; the probability for such a chance occurrence at two dose points is less than 0.001.
Result	:	Resorcinol induced SCE at doses of 167 and 500 µg/mL in the absence of S9 and at 1,670 and 5,000 µg/mL in the presence of Aroclor 1254-induced male Sprague-Dawley rat liver S9.
Reference	:	NTP Technical Report on the Toxicology and Carcinogenesis Studies of Resorcinol (CAS No. 108-46-3) in F344/N Rats and B6C3F$_1$ Mice (Gavage Studies) NIH Publication No. 91-2858
Reliability	:	(1) valid without restriction
13.09.2005		(1)
Type	:	Ames test
System of testing	:	Salmonella tuphimrium TA1538
Test concentration	:	No data
Cycotoxic concentr.	:	No data
Metabolic activation	:	with and without
Result	:	Negative
Method	:	other: Hoechst Ag Internal Directive, 1977
Year	:	No data
GLP	:	No data
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(4) not assignable
14.09.2005		(50)
Type	:	Ames test
System of testing	:	Salmonella typhimrium TA 98, TA 100, TA 1535, TA 1537, TA 1538
Test concentration	:	No data
Cycotoxic concentr.	:	No data
Metabolic activation	:	with and without
Result	:	Negative
Method	:	No data
Year	:	No data
GLP	:	No data

Test substance	:	No data
Remark	:	5-1000 µg/plate, 3 plates/concentration, independent repetition; cytotoxic range not included negative for both with and without metabolic activation.
Reliability	:	(4) not assignable

14.09.2005 (111)

Type	:	Cytogenetic assay
System of testing	:	Peripheral human lymphocytes
Test concentration	:	20-100 µg/ml; 800 metaphases assessed
Cycotoxic concentr.	:	No data
Metabolic activation	:	Without
Result	:	Positive
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Remark	:	Concentration-dependent increase in the aberration rate.
Reliability	:	(4) not assignable

14.09.2005 (25)

Type	:	Cytogenetic assay
System of testing	:	Ovarial cells of the Chinese hamster (CHO)
Test concentration	:	1600 µg/ml; 200 metaphases assessed
Cycotoxic concentr.	:	No data
Metabolic activation	:	with and without
Result	:	Positive
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Reliability	:	(4) not assignable

14.09.2005 (121)

Type	:	Cytogenetic assay
System of testing	:	Peripheral human lymphocytes
Test concentration	:	80-320 µg/ml
Cycotoxic concentr.	:	100 metaphases/concentration
Metabolic activation	:	without
Result	:	negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Reliability	:	(4) not assignable

14.09.2005 (25)

Type	:	Cytogenetic assay
System of testing	:	Ovarial cells of the Chinese hamster (CHO)
Test concentration	:	400-1600 µg/ml
Cycotoxic concentr.	:	200 metaphases assessed
Metabolic activation	:	with and without
Result	:	negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Reliability	:	(4) not assignable

14.09.2005 (25)

Type	:	Ames test
System of testing	:	salmonella typhimrium TA98, TA100, TA1535, TA1537
Test concentration	:	No data
Cycotoxic concentr.	:	No data
Metabolic activation	:	With
Result	:	Negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Remark	:	200-500 µg/plate; 3 plates/concentration; independent repetition; cytotoxic range included.
Reliability	:	(4) not assignable

14.09.2005 (22)

Type	:	Ames test
System of testing	:	Salmonella typhimrium TA98
Test concentration	:	No data
Cycotoxic concentr.	:	No data
Metabolic activation	:	with and without
Result	:	negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Remark	:	Concentrations of 10-30 µg/plate; no information on cytotoxic range
Reliability	:	(4) not assignable

14.09.2005 (134)

Type	:	Ames test
System of testing	:	Escherichia coli WP@, WP2uvrA-
Test concentration	:	No data
Cycotoxic concentr.	:	No data
Metabolic activation	:	with and without
Result	:	Negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Reliability	:	(4) not assignable

14.09.2005 (100)

Type	:	Ames test
System of testing	:	Salmonella typhimrium TA98, TA100, TA1535, TA1537,TA1538
Test concentration	:	No data
Cycotoxic concentr.	:	No data
Metabolic activation	:	with and without
Result	:	Negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Remark	:	5-1000 µg/plate, 3 plates/concentration, independent repetition; cytotoxic range not included.
Reliability	:	(4) not assignable

14.09.2005 (111)

Type	:	Ames test
System of testing	:	Salmonella typhimrium TA98, TA100, TA1535, TA1537
Test concentration	:	No data
Cycotoxic concentr.	:	No data
Metabolic activation	:	With
Result	:	Negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Remark	:	10-1000 µg/plate; no information on cytotoxic range
Reliability	:	(4) not assignable
14.09.2005		(84)

Type	:	Ames test
System of testing	:	Salmonella typhimrium TA98, TA100, TA1535, TA1537, TA1538
Test concentration	:	No data
Cycotoxic concentr.	:	No data
Metabolic activation	:	with and without
Result	:	Positive
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Remark	:	Concentration up to 3600 µg/plate; in ZLM medium: TA100: -S9 positive, +S9 ambiguous TA1535: -S9 negative, +S9 positive In other strains: negative
Reliability	:	(4) not assignable
14.09.2005		(41)

Type	:	Ames test
System of testing	:	Salmonella typhimrium TA100, TA1538
Test concentration	:	No data
Cycotoxic concentr.	:	No data
Metabolic activation	:	Without
Result	:	Negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Remark	:	3.3-3000 µg/plate
Reliability	:	(4) not assignable
14.09.2005		(38)

Type	:	Ames test
System of testing	:	Salmonella typhimrium TA98
Test concentration	:	No data
Cycotoxic concentr.	:	No data
Metabolic activation	:	with and without
Result	:	Negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data

Remark : 500-2000 µg/plate; 3 plates/concentration
Reliability : (4) not assignable
14.09.2005 (23)

Type : Cytogenetic assay
System of testing : Human lymphocytes
Test concentration : No data
Cycotoxic concentr. : No data
Metabolic activation : no data
Result : Positive
Method : No data
Year : No data
GLP : No data
Test substance : No data

Remark : Abstract
Reliability : (4) not assignable
14.09.2005 (73)

Type : Cytogenetic assay
System of testing : Fibroblasts of the Chinese hamster (CHL)
Test concentration : No data
Cycotoxic concentr. : No data
Metabolic activation : without
Result : Positive
Method : No data
Year : No data
GLP : No data
Test substance : No data

Remark : With metabolic activation (S9 mix), reduction inclastogenic effect (abstract)
Reliability : (4) not assignable
14.09.2005 (106)

Type : Mitotic recombination in Saccharomyces cerevisiae
System of testing : Saccharomyces cerevisiae D7
Test concentration : 1000 µg/ml
Cycotoxic concentr. : No data
Metabolic activation : Without
Result : Ambiguous
Method : No data
Year : No data
GLP : No data
Test substance : No data

Remark : At pH of 7 test substance: negative
At pH of 10 test substance: positive
Reliability : (4) not assignable
14.09.2005 (105)

Type : Cytogenetic assay
System of testing : Human lymphocytes
Test concentration : No data
Cycotoxic concentr. : No data
Metabolic activation : no data
Result : Positive
Method : No data
Year : No data
GLP : No data
Test substance : No data

Remark : Abstract

Reliability : (4) not assignable
14.09.2005 (57)

Type : Cytogenetic assay
System of testing : Human fibroblasts
Test concentration : No data
Cycotoxic concentr. : No data
Metabolic activation : No data
Result : positive
Method : No data
Year : No data
GLP : No data
Test substance : No data

Remark : Abstract
Reliability : (4) not assignable
26.05.2004 (57)

Type : Cytogenetic assay
System of testing : Human embryo cells
Test concentration : No data
Cycotoxic concentr. : No data
Metabolic activation : no data
Result : positive
Method : No data
Year : No data
GLP : No data
Test substance : No data

Remark : Embryo cells obtained from amniotic fluid (abstract)
Reliability : (4) not assignable
14.09.2005 (57)

Type : Cytogenetic assay
System of testing : Human lymphocytes
Test concentration : No data
Cycotoxic concentr. : No data
Metabolic activation : no data
Result : positive
Method : No data
Year : No data
GLP : No data
Test substance : No data

Remark : Abstract
Reliability : (4) not assignable
14.09.2005 (108)

Type : Cytogenetic assay
System of testing : Human fibroblasts
Test concentration : 12-50 µg/ml
Cycotoxic concentr. : 100 metaphases/concentration
Metabolic activation : without
Result : negative
Method : No data
Year : No data
GLP : No data
Test substance : No data

Reliability : (4) not assignable
14.09.2005 (25)

Type	:	Cytogenetic assay
System of testing	:	Peripheral human lymphocytes
Test concentration	:	80-220 µg/ml
Cycotoxic concentr.	:	No data
Metabolic activation	:	no data
Result	:	positive
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Remark	:	Reduced mitosis rate, chromosome aberrations (up to approx. 60% of the metaphases damaged, primarily chromatid breaks)
Reliability	:	(4) not assignable

14.09.2005 (109)

Type	:	Mouse lymphoma assay
System of testing	:	No data
Test concentration	:	125-5000 ug/ml; concentration dependent
Cycotoxic concentr.	:	No data
Metabolic activation	:	without
Result	:	positive
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Remark	:	Significant increase in mutant numbers in 3 independent runs
Reliability	:	(4) not assignable

14.09.2005 (85)

Type	:	other: Cell transformation
System of testing	:	Kidney cells of the Syrian hamster (BHK 21/c1 13, Human fibroblasts (WI-38) Human liver cells (Chang)
Test concentration	:	No data
Cycotoxic concentr.	:	No data
Metabolic activation	:	no data
Result	:	negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Reliability	:	(4) not assignable

14.09.2005 (102)

Type	:	other: DNA-Alkaline-elution test
System of testing	:	Rat hepatocytes
Test concentration	:	No data
Cycotoxic concentr.	:	No data
Metabolic activation	:	no data
Result	:	positive
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Reliability	:	(4) not assignable

14.09.2005 (132)

Type	:	other: DNA-cell binding (DCB) assay
System of testing	:	Escherichia coli Q 13

Test concentration	:	No data
Cycotoxic concentr.	:	No data
Metabolic activation	:	no data
Result	:	negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Remark	:	With lysosyme and liver extract
Reliability	:	(4) not assignable

14.09.2005 (74)

Type	:	Sister chromatid exchange assay
System of testing	:	Human lymphocytes
Test concentration	:	Up to 27.5 µg/ml
Cycotoxic concentr.	:	25 metaphases/concentration assessed
Metabolic activation	:	no data
Result	:	negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Reliability	:	(4) not assignable

14.09.2005 (65)

Type	:	Unscheduled DNA synthesis
System of testing	:	Primary rat hepatocytes
Test concentration	:	110 µg/ml (maximum non-cytoxic concentration)
Cycotoxic concentr.	:	No data
Metabolic activation	:	no data
Result	:	negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Reliability	:	(4) not assignable

14.09.2005 (100)

Type	:	Sister chromatid exchange assay
System of testing	:	V 79-cells of the Chinese hamster
Test concentration	:	0.55-2.2 µg/ml
Cycotoxic concentr.	:	No data
Metabolic activation	:	without
Result	:	negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Remark	:	Abstract
Reliability	:	(4) not assignable

14.09.2005 (137)

Type	:	Sister chromatid exchange assay
System of testing	:	Peripheral human lymphocytes
Test concentration	:	20-100 µg/ml
Cycotoxic concentr.	:	400 metaphases/concentration assessed
Metabolic activation	:	without
Result	:	negative

Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data

Reliability	:	(4) not assignable
14.09.2005		(25)

Type	:	Sister chromatid exchange assay
System of testing	:	Ovarial cells of the Chinese hamster (CHO)
Test concentration	:	50-1600 µg/ml
Cycotoxic concentr.	:	50-75 metaphases/concentration assessed
Metabolic activation	:	without
Result	:	negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data

Reliability	:	(4) not assignable
14.09.2005		(25)

Type	:	Sister chromatid exchange assay
System of testing	:	Ovarial cells of the Chinese hamster (CHO)
Test concentration	:	400-1600 µg/l
Cycotoxic concentr.	:	75-100 metaphases/concentration assessed
Metabolic activation	:	with and without
Result	:	negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data

Reliability	:	(4) not assignable
14.09.2005		(25)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	Drosophila SLRL test
Species	:	Drosophila melanogaster
Sex	:	male
Strain	:	other: Canton-s wild type
Route of admin.	:	other:feed exposure or injection
Exposure period	:	72 hours
Doses	:	11,000 ppm for feeding 11,940 ppm by injection
Result	:	ambiguous
Method	:	other:Zimmering et al (1985)
Year	:	1991
GLP	:	no data
Test substance	:	Other TS: see remark

Test substance	:	Resorcinol sent as a coded aliquot from Radian Corporation (Austin, TX)
Method		Initially, the study chemical was assayed in the sex-linked recessive lethal (SLRL) test by feeding for 3 days to adult Canton-S wild-type males no more than 24 hours old at the beginning of treatment. Because no response was obtained, the chemical was retested by injection into adult males. To administer a chemical by injection, a glass Pasteur pipette was drawn out in a flame to a microfine filament and the tip was broken off to allow delivery of the test solution. Injection was performed either manually,

by attaching a rubber bulb to the other end of the pipette and forcing through sufficient solution (0.2 to 0.3 µL) to slightly distend the abdomen of the fly, or by attaching the pipette to a microinjector which automatically delivers a calibrated volume. Flies are anesthetized with ether and immobilized on a strip of double stick tape; the chemical was injected into the thorax under the wing with the aid of a dissecting microscope.

Toxicity tests were performed to set concentrations of study chemical at a level which would induce 30% mortality after 72 hours of feeding or 24 hours after injection, while keeping induced sterility at an acceptable level. For the SLRL test, exposure by feeding was done by allowing Canton-S males (10 to 20 flies/vial) to feed for 72 hours on a solution of the study chemical in 5% sucrose. In the injection experiments, 24- to 72-hour-old Canton-S males were treated with a solution of the chemical dissolved in 0.7% saline and were allowed to recover for 24 hours. Exposed males were mated to three *Basc* females for 3 days and given fresh females at 2-day intervals to produce three matings of 3, 2, and 2 days; sample sperm from successive matings were treated at successively earlier post-meiotic stages. F_1 heterozygous females were allowed to mate with their siblings and were then placed in individual vials. F_2 daughters from the same parental male were kept together to identify clusters. (A cluster occurs when a number of mutants from a given male result from a single spontaneous premeiotic mutation event, and is identified when the number of mutants from that male exceeds the number predicted by a Poisson distribution). If a cluster was identified, all data from the male in question were discarded. After 17 days, presumptive lethal mutations were identified as occurring in vials containing no wild-type males; these were retested. A minimum of two experiments were performed for each study chemical, resulting in the testing of approximately 5,000 treated and 5,000 control chromosomes. The only exceptions occurred when the results of the first experiment were clearly positive (induced frequency of recessive lethal mutations equal to or greater than 1%); then, the second trial was not run.

Recessive lethal data were analyzed by the normal approximation to the binomial test (Margolin *et al.,* 1983). A test result was considered to be positive if the P value was less than 0.01 and the mutation frequency in the tested group was greater that 0.10%, or if the P value was less than 0.05 and the frequency in the treatment group was greater than 0.15%. A test was considered to be inconclusive if (a) the P value was between 0.05 and 0.01 but the frequency in the treatment group was between 0.10% and 0.15%, or (b) the P value was between 0.10 and 0.05 but the frequency in the treatment group was greater than 0.10%. A result was considered to be negative if the P value was greater than 0.10 or if the frequency in the treatment group was less than 0.10%.

Result : Resorcinol (11,000 ppm) was negative for induction of sex-linked recessive lethal mutations in germ cells of male Drosophila melangaster when administered to adult flies by feeding. Administration of the test substance (11,940) by injection yielded an increase in mutations which was equivocal (P=0.06 and mutation frequency of 0.12% in the treated group).

Reference : NTP Technical Report on the Toxicology and Carcinogenesis Studies of Resorcinol (CAS No. 108-46-3) in F344/N Rats and B6C3F_1 Mice (Gavage Studies) NIH Publication No. 91-2858

Reliability : (1) valid without restriction
13.09.2005 (1)

Type : Drosophila SLRL test
Species : Drosophila melanogaster
Sex : male/female
Strain : No data
Route of admin. : oral feed

Exposure period	:	No data
Doses	:	5506 µg/ml
Result	:	Negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data

Reliability : (4) not assignable
14.09.2005 (41)

Type	:	Inhibition of DNA-Synthesis
Species	:	mouse
Sex	:	No data
Strain	:	No data
Route of admin.	:	oral unspecified
Exposure period	:	No data
Doses	:	100 mg/kg bw
Result	:	negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data

Reliability : (4) not assignable
14.09.2005 (110)

Type	:	Micronucleus assay
Species	:	mouse
Sex	:	male/female
Strain	:	No data
Route of admin.	:	i.p.
Exposure period	:	2 days
Doses	:	55, 110, 220 mg/kg bw
Result	:	negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data

Remark : 2 animals/sex/dose; time of preparation: 30h; 1000 polychromatic erythrocytes per animal assessed.
Reliability : (4) not assignable
14.09.2005 (41)

Type	:	Micronucleus assay
Species	:	mouse
Sex	:	male/female
Strain	:	No data
Route of admin.	:	i.p.
Exposure period	:	No data
Doses	:	75 mg/kg bw
Result	:	negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data

Remark : 5 animals/dose or control group/time of preparation 24, 48, 72 or 96h; 1000 polychromatic erythrocytes per animal assessed.
Reliability : (4) not assignable
14.09.2005 (94)

Type	:	Micronucleus assay
Species	:	mouse
Sex	:	male
Strain	:	No data
Route of admin.	:	i.p.
Exposure period	:	No data
Doses	:	37.5-300 mg/kg bw
Result	:	Negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Remark	:	4 animals/dose; time of preparation 24 or 48h; 1000 polychromatic erythrocytes per animal assessed.
Reliability	:	(4) not assignable

14.09.2005 (25)

Type	:	Micronucleus assay
Species	:	mouse
Sex	:	male
Strain	:	No data
Route of admin.	:	i.p.
Exposure period	:	No data
Doses	:	55-220 mg/kg bw
Result	:	negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Reliability	:	(4) not assignable

14.09.2005 (138)

Type	:	Micronucleus assay
Species	:	rat
Sex	:	male/female
Strain	:	No data
Route of admin.	:	oral unspecified
Exposure period	:	2 days
Doses	:	250 mg/kg bw
Result	:	Negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Remark	:	5 animals/sex/dose; time of preparation: 30h; 2000 polychomatic erythrocytes per animal assessed.
Reliability	:	(4) not assignable

14.09.2005 (59)

Type	:	Sister chromatid exchange assay
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	dermal
Exposure period	:	20 minutes
Doses	:	0.2, 2, 20, 100, 200, 300 mg/kg bw
Result	:	negative
Method	:	No data

Year	:	No data
GLP	:	No data
Test substance	:	No data
Remark	:	2-3 animals/dose; time of preparation: 24h; 20-54 metaphases analyzed per animal.
Reliability	:	(4) not assignable

14.09.2005 (10)

Type	:	Sister chromatid exchange assay
Species	:	rat
Sex	:	male/female
Strain	:	No data
Route of admin.	:	i.p.
Exposure period	:	No data
Doses	:	1-100 mg/kg bw
Result	:	negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Remark	:	1-3 animals/dose; time of preparation: 24 h; 13-36 metaphases analyzed per animal.
Reliability	:	(4) not assignable

14.09.2005 (10)

Type	:	Sister chromatid exchange assay
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	oral unspecified
Exposure period	:	No data
Doses	:	0.8, 4, 20, 100 mg/kg bw
Result	:	negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Remark	:	3 animals/dose; time of preparation: 24 h; 12-54 metaphases analyzed per animal.
Reliability	:	(4) not assignable

14.09.2005 (10)

Type	:	other: Sperm Abnormality test
Species	:	mouse
Sex	:	male
Strain	:	No data
Route of admin.	:	i.p.
Exposure period	:	No data
Doses	:	55-220 mg/kg bw
Result	:	negative
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Reliability	:	(4) not assignable

14.09.2005 (138)

5.7 CARCINOGENICITY

Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	gavage
Exposure period	:	104 weeks
Frequency of treatm.	:	Daily: 5 days a week
Post exposure period	:	No data
Doses	:	0, 112, 225 mg/kg bw (males) 0, 50, 100 150 mg/kg (females)
Result	:	negative
Control group	:	yes
Method	:	other:NTP Board EPA/FDA guidelines
Year	:	1991
GLP	:	yes
Test substance	:	Other TS: see remark

Test substance : Obtained from NAPP Chemicals, Incorporated. Preparation in water, purity >99% Lot No. IN-79-7087

Method : Groups of 60 male rats were administered 0, 112 or 225 mg/kg resorcinol in deionized water by gavage. The rats were 6-7 weeks at start of study. Groups of 60 females rats were initially administered the same doses as the male rats , but by week 22 of the study, 16 of the high dose females had died. Consequently, the female rat study was restarted using doses of 0, 50, 100 or 150 mg/kg. Doses were given at a volume of 5ml/kg, 5 days a week for 103 weeks.

Animal Maintenance
Both rats and mice were housed five to a cage with feed and drinking water available ad libitum. Cages within racks were rotated once a week and positions of the racks within the room were changed once every 2 weeks

Clinical Examinations and Pathology
All animals were observed twice daily. Clinical signs of toxicity were recorded every 4 weeks. Individual body weights were obtained weekly for the first 13 weeks and every 4 weeks thereafter until the last 3 months of the studies, when body weights were recorded every 2 weeks. After 15 months on study, 10 male and 10 female rats from each dose group were sacrificed for evaluation of organ weights, hematology, and clinical chemistry.Parameters measured were:
Hematology: hematocrit, hemoglobin, erythrocytes, mean cell volume, mean cell hemoglobin, mean cell hemoglobin concentration, leukocytes, segmented neutrophils, lymphocytes, monocytes, eosinophils, and nucleated erythrocytes. Clinical chemistry: urea nitrogen, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, and sorbitol dehydrogenase.

A necropsy was performed on all animals. During necropsy, all organs and tissues were examined for grossly visible lesions. Organ weights recorded for all brain, right kidney and liver of all animals sacrificed at 15 months except male rats receiving 225 mg/kg.

Complete histologic examination was conducted on all control and high-dose male rats from the 15-month study and all rats from the 2-year study. Gross lesions only were examined from low-dose male rats and all female rats from the 15-month studies. In addition to tissue masses and gross lesions, the following organs and/or tissues were included in complete histopathologic examinations: adrenal glands, aorta, bone (femur including marrow), brain, clitoral gland (rats), epididymis, esophagus, eye (if grossly abnormal), heart, kidneys, large intestine (cecum, colon,

rectum), liver, lungs, mammary gland, mesenteric lymph node, nasal cavity, ovaries, pancreas, parathyroids, pituitary, preputial gland (rats), prostate, salivary gland, skin, small intestine (duodenum, jejunum, ileum), spleen, stomach, testes, thymus, thyroids, trachea, urinary bladder, and uterus.

Pathology evaluations were completed by the study laboratory pathologist and the pathology data were entered into the Toxicology Data Management System (TDMS). The slides, paraffin blocks, and residual wet tissues were sent to the NTP Archives for inventory, slide/block match, and wet tissue audit for accuracy of labeling and animal identification and for thoroughness of tissue trimming. The slides, individual animal data records, and pathology tables were evaluated by an independent quality assessment laboratory. The individual animal records and tables were compared for accuracy, slides and tissue counts were verified, and histotechnique was evaluated. A quality assessment pathologist reviewed selected tissues from the 15-month and 2-year studies for accuracy and consistency of lesion diagnosis. All diagnosed neoplasms in all animals, brains from all male rats were reviewed. In addition, all tissues were examined from six rats of each sex randomly selected from each control and high-dose group in the 15-month studies, and from five rats of each sex randomly selected from each control and high-dose group in the 2-year studies.

The quality assessment report and slides were submitted to a PWG chairperson, who reviewed tissues for which there was a disagreement in diagnosis between the laboratory and quality assessment pathologists. Representative examples of nonneoplastic lesions and neoplasms and examples of disagreements in diagnosis between the laboratory and quality assessment pathologists were reviewed by the PWG. Each PWG included the quality assessment pathologist as well as other pathologists experienced in rodent toxicologic pathology, who examined these tissues without knowledge of dose group or previously rendered diagnoses. When the consensus diagnosis of a PWG differed from that of the laboratory pathologist, the final diagnosis was changed to reflect the opinion of the PWG. Details of these review procedures have been described, in part, by Maronpot and Boorman (1982) and Boorman et al (1985). For subsequent analysis of pathology data, the diagnosed lesions for each tissue type are evaluated separately or combined according to the guidelines of McConnell et al (1986).

Statistical Methods
Survival Analyses
The probability of survival was estimated by the product-limit procedure of Kaplan and Meier (1958) and is presented in the Results section of this report. Animals were censored from the survival analyses at the time they were found dead from other than natural causes or were found missing; animals dying from natural causes were not censored. Statistical analyses for possible dose-related effects on survival used Cox's (1972) method for testing two groups for equality and Tarone's (1975) life table tests to identify dose-related trends. All reported P values for the survival analysis are two-sided.

Calculation of Incidence.
The incidence of neoplastic or nonneoplastic lesions is given as the ratio of the number of animals bearing such lesions at a specific anatomic site to the number of animals in which that site was examined. In most instances, the denominators include only those animals for which the site was examined histologically. However, when macroscopic examination was required to detect lesions (e.g., skin or mammary tumors) before tissue sampling for histopathology, or when lesions could have appeared at multiple sites (e.g., mononuclear cell leukemia), the denominators consist of the number of animals on which a necropsy was performed.

Analysis of Tumor Incidence
The majority of tumors in these studies were considered to be incidental to the cause of death or not rapidly lethal. Thus, the primary statistical method used was a logistic regression analysis, which assumed that the diagnosed tumors were discovered as the result of death from an unrelated cause and, thus, did not affect the risk of death. In this approach, tumor prevalence was modeled as a logistic function of chemical exposure and time. Both linear and quadratic terms in time were incorporated initially, and the quadratic term was eliminated if it did not significantly enhance the fit of the model. The dosed and control groups were compared on the basis of the likelihood score test for the regression coefficient of dose. This method of adjusting for intercurrent mortality is the prevalence analysis of Dinse and Lagakos (1983), further described and illustrated by Dinse and Haseman (1986). When tumors are incidental, this comparison of the time-specific tumor prevalences also provides a comparison of the time-specific tumor incidences (McKnight and Crowley, 1984).

In addition to logistic regression, alternative methods of statistical analysis were used. These include the life table test (Cox, 1972; Tarone, 1975), appropriate for rapidly lethal tumors, and the Fisher exact test and the Cochran-Armitage trend test (Armitage, 1971; Gart et al., 1979), procedures based on the overall proportion of tumor-bearing animals.

Tests of significance include pairwise comparisons of each dosed group with controls and a test for an overall dose-response trend. Continuity-corrected tests were used in the analysis of tumor incidence, and reported P values are one-sided. The procedures described above also were used to evaluate selected nonneoplastic lesions.
Historical Control Data
Although the concurrent control group is always the first and most appropriate control group used for evaluation, historical control data can be helpful in the overall assessment of tumor incidence. Consequently, control tumor incidences from the NTP historical control data base (Haseman et al., 1984, 1985) are included in the NTP reports for tumors appearing to show compound-related effects.

Analysis of Continuous Variables
Two approaches were employed to assess the significance of pairwise comparisons between dosed and control groups in the analysis of continuous variables. Organ and body weight data, which have approximately normal distributions, were analyzed using the parametric multiple comparison procedures of Williams (1971, 1972) and Dunnett (1955). Clinical chemistry and hematology data, which have typically skewed distributions, were analyzed using the nonparametric multiple comparison methods of Shirley (1977) and Dunn (1964). Jonckheere's test (Jonckheere, 1954) was used to assess the significance of the dose-response trends and to determine whether a trend-sensitive test (Williams' or Shirley's test) was more appropriate for pairwise comparisons than a test that does not assume a monotonic dose-response trend (Dunnett's or Dunn's test).

Quality Assurance Methods
The 2-year studies were conducted in compliance with FDA Good Laboratory Practice Regulations (21 CFR Part 58). In addition, as study records were submitted to the NTP Archives, they were audited retrospectively by an independent quality assurance contractor. Separate audits covering completeness and accuracy of the pathology data, pathology specimens, final pathology tables, and preliminary review draft of this NTP Technical Report were conducted. Audit procedures are presented in the reports, which are on file at the NIEHS. The audit findings were reviewed and assessed by the NTP staff so that all had been

resolved or were otherwise addressed during the preparation of this Technical Report.

Result : Tumor type and incidence were in the same range as those of the control. Body weight development of the animals in the high dose group was retarted by 10-15% from week 87 onwards. The mortality in the high dose group was significantly higher than in the control group (no further information). The clinical symptoms included the following: ataxia, abdominal or lateral position and tremours.

15-Month Interim Evaluations
Ten rats of each sex in each dose, group were predesignated for interim evaluations at 15 months. Due to early mortality in the high-dose males, animals from this group were not sacrificed at 15 months. Instead, 10 high-dose males that died or were sacrificed in a moribund condition near month 15 were included in the interim evaluation. Relative brain weight was significantly increased for males receiving 112 mg/kg and relative liver weight was significantly increased for females receiving 150 mg/kg. These differences in relative weights were considered to be associated with the decreased body weights in these groups. No treat-ment-related differences in hematology or clinical chemistry parameters were seen. No treatment-related neoplasms or nonneoplastic lesions were found during histopathologic examination.

Body Weights and Clinical Findings
The mean body weights of males and females receiving 150 or 225 mg/kg were lower than those of the controls throughout the studies. Males given 225 mg/kg had body weights 10% to 15% lower than those of the control from week 87 to study termination. Females given 150 mg/kg had mean body weights from 11% to 14% lower than those of the controls from week 95 to study termination. The mean body weights of males and females receiving the low doses were similar to those of the controls. Clinical findings including ataxia, prostration, salivation, and tremors were seen in treated males and in females receiving 100 and 150 mg/kg. These clinical signs of toxicity began shortly after chemical administration lasting from 30 minutes to an hour and became more pronounced at the end of each 5-day dose period.

Survival
The survival of high-dose males and females was significantly lower than that of the control. The remaining dose groups had survival rates similar to those of the controls.

Sentinel Animals
Positive serological titers for Sendai virus and rat corona virus/ sialodacryoadenitis were found in sentinel animals at 6, 12, 18, and 24 months. However, there was no clinical or histopathologic evidence of disease.

Pathology and Statistical Analysis of Results
Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, and statistical analyses of primary tumors that occurred with an incidence of at least 5% in at least one animal group mentioned in this section are presented in Appendixes A and B of the report for male and female rats.

Administration of resorcinol by gavage to male and female F344/N rats for 2 years did not result in any statistically or biologically significant increases in the incidences of neoplasms or nonneoplastic lesions at any site. Incidences of a variety of neoplasms in high-dose males and nonneoplastic lesions in high-dose males and females were decreased as compared with controls due to the lower survival in the dosed groups

Reference : NTP Technical Report on the Toxicology and Carcinogenesis Studies of

Resorcinol (CAS No. 108-46-3) in F344/N Rats and B6C3F$_1$ Mice (Gavage Studies) NIH Publication No. 91-2858

Reliability : (1) valid without restriction
14.09.2005 (1)

Species	:	mouse
Sex	:	male/female
Strain	:	B6C3F1
Route of admin.	:	gavage
Exposure period	:	104 weeks
Frequency of treatm.	:	Daily:5 days a week
Post exposure period	:	No data
Doses	:	0, 112, 225 mg/kg bw
Result	:	negative
Control group	:	yes
Method	:	other: NTP board EPA/FDA guidelines
Year	:	1991
GLP	:	yes
Test substance	:	Other TS: see remark

Test substance : Obtained from NAPP Chemicals, Incorporated. Preparation in water, purity >99% Lot No. IN-79-7087

Method : Groups of 60 mice of each sex were administered 0, 112, or 225 mg/kg resorcinol in deionized water by gavage.

Ten mice of each sex per dose group were designated for interim evaluations (organ weights, hematology, clinical chemistry, and histopathology) after 15 months (66 weeks) of chemical administration.

Mice were 7 to 8 weeks old of start of study mice were housed five to a cage with feed and drinking water available ad libitum. Cages within racks were rotated once a week and positions of the racks within the room were changed once every 2 weeks

Clinical Examinations and Pathology
All animals were observed twice daily. Clinical signs of toxicity were recorded every 4 weeks. Individual body weights were obtained weekly for the first 13 weeks and every 4 weeks thereafter until the last 3 months of the studies, when body weights were recorded every 2 weeks. After 15 months on study, 10 male and 10 female mice from each dose group were sacrificed for evaluation of organ weights, hematology, and clinical chemistry. Parameters measured were: *Hematolgy:* hematocrit, hemoglobin, erythrocytes, mean cell volume, mean cell hemoglobin, mean cell hemoglobin concentration, leukocytes, segmented neutrophils, lymphocytes, monocytes, eosinophils, and nucleated erythrocytes. Clinical chemistry: urea nitrogen, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, and sorbitol dehydrogenase.

A necropsy was performed on all animals. During necropsy, all organs and tissues were examined for grossly visible lesions.
Complete histologic examination was conducted all mice from the 15-month studies, and all control and high-dose mice from the 2-year studies. Only tissues containing gross lesions observed at necropsy were examined from the low-dose mouse groups from the 15-month and 2-year studies.. In addition to tissue masses and gross lesions, the following organs and/or tissues were included in complete histopathologic examinations: adrenal glands, aorta, bone (femur including marrow), brain, epididymis, esophagus, eye (if grossly abnormal), gallbladder (mice), heart, kidneys, large intestine (cecum, colon, rectum), liver, lungs, mammary gland, mesenteric lymph node, nasal cavity, ovaries, pancreas, parathyroids, pituitary, prostate, salivary gland, skin, small intestine (duodenum, jejunum,

ileum), spleen, stomach, testes, thymus, thyroids, trachea, urinary bladder, and uterus.

Pathology evaluations were completed by the study laboratory pathologist and the pathology data were entered into the Toxicology Data Management System (TDMS). The slides, paraffin blocks, and residual wet tissues were sent to the NTP Archives for inventory, slide/block match, and wet tissue audit for accuracy of labeling and animal identification and for thoroughness of tissue trimming. The slides, individual animal data records, and pathology tables were evaluated by an independent quality assessment laboratory. The individual animal records and tables were compared for accuracy, slides and tissue counts were verified, and histotechnique was evaluated. A quality assessment pathologist reviewed selected tissues from the 15-month and 2-year studies for accuracy and consistency of lesion diagnosis. All diagnosed neoplasms in all animals, and forestomachs from all female mice were reviewed. In addition, all tissues were examined from six mice of each sex randomly selected from each control and high-dose group in the 15-month studies, and from five mice of each sex randomly selected from each control and high-dose group in the 2-year studies.

The quality assessment report and slides were submitted to a PWG chairperson, who reviewed tissues for which there was a disagreement in diagnosis between the laboratory and quality assessment pathologists. Representative examples of nonneoplastic lesions and neoplasms and examples of disagreements in diagnosis between the laboratory and quality assessment pathologists were reviewed by the PWG. Each PWG included the quality assessment pathologist as well as other pathologists experienced in rodent toxicologic pathology, who examined these tissues without knowledge of dose group or previously rendered diagnoses. When the consensus diagnosis of a PWG differed from that of the laboratory pathologist, the final diagnosis was changed to reflect the opinion of the PWG. Details of these review procedures have been described, in part, by Maronpot and Boorman (1982) and Boorman et aL (1985). For subsequent analysis of pathology data, the diagnosed lesions for each tissue type are evaluated separately or combined according to the guidelines of McConnell et aL (1986).

Statistical Methods
Survival Analyses
The probability of survival was estimated by the product-limit procedure of Kaplan and Meier (1958) and is presented in the Results section of this report. Animals were censored from the survival analyses at the time they were found dead from other than natural causes or were found missing; animals dying from natural causes were not censored. Statistical analyses for possible dose-related effects on survival used Cox's (1972) method for testing two groups for equality and Tarone's (1975) life table tests to identify dose-related trends. All reported P values for the survival analysis are two-sided.

Calculation of Incidence.
The incidence of neoplastic or nonneoplastic lesions is given as the ratio of the number of animals bearing such lesions at a specific anatomic site to the number of animals in which that site was examined. In most instances, the denominators include only those animals for which the site was examined histologically. However, when macro-scopic examination was required to detect lesions (e.g., skin or mammary tumors) before tissue sampling for histopathology, or when lesions could have appeared at multiple sites (e.g., mononuclear cell leukemia), the denominators consist of the number of animals on which a necropsy was performed.

Analysis of Tumor Incidence
The majority of tumors in these studies were con-sidered to be incidental to the cause of death or not rapidly lethal. Thus, the primary statistical method used was a logistic regression analysis, which assumed that the diagnosed tumors were discovered as the result of death from an unrelated cause and, thus, did not affect the risk of death. In this approach, tumor prevalence was modeled as a logistic function of chemical exposure and time. Both linear and quadratic terms in time were incorporated initially, and the quadratic term was eliminated if it did not significantly enhance the fit of the model. The dosed and control groups were compared on the basis of the likelihood score test for the regression coefficient of dose. This method of adjusting for intercurrent mortality is the prevalence analysis of Dinse and Lagakos (1983), further described and illustrated by Dinse and Haseman (1986). When tumors are incidental, this comparison of the time-specific tumor prevalences also provides a comparison of the time-specific tumor incidences (McKnight and Crowley, 1984).

In addition to logistic regression, alternative methods of statistical analysis were used, These include the life table test (Cox, 1972; Tarone, 1975), appropriate for rapidly lethal tumors, and the Fisher exact test and the Cochran-Armitage trend test (Armitage, 1971; Gart et al., 1979), procedures based on the overall proportion of tumor-bearing animals.

Tests of significance include pairwise comparisons of each dosed group with controls and a test for an overall dose-response trend. Continuity-corrected tests were used in the analysis of tumor incidence, and reported P values are one-sided. The proce-dures described above also were used to evaluate selected nonneoplastic lesions. For further discussion of these statistical methods, see Haseman, 1984.

Historical Control Data
Although the concurrent control group is always the first and most appropriate control group used for evaluation, historical control data can be helpful in the overall assessment of tumor incidence. Conse-quently, control tumor incidences from the NTP historical control data base (Haseman et al., 1984, 1985) are included in the NTP reports for tumors appearing to show compound-related effects.

Analysis of Continuous Variables
Two approaches were employed to assess the signif-icance of pairwise comparisons between dosed and control groups in the analysis of continuous variables. Organ and body weight data, which have approximately normal distributions, were analyzed using the parametric multiple comparison proce-dures of Williams (1971, 1972) and Dunnett (1955). Clinical chemistry and hematology data, which have typically skewed distributions, were analyzed using the nonparametric multiple comparison methods of Shirley (1977) and Dunn (1964). Jonckheere's test (Jonckheere, 1954) was used to assess the signifi-cance of the dose-response trends and to determine whether a trend-sensitive test (Williams' or Shirley's test) was more appropriate for pairwise comparisons than a test that does not assume a monotonic dose-response trend (Dunnett's or Dunn's test).

Quality Assurance Methods
The 13-week and 2-year studies were conducted in compliance with FDA Good Laboratory Practice Regulations (21 CFR Part 58). In addition, as study records were submitted to the NTP Archives, they were audited retrospectively by an independent quality assurance contractor. Separate audits cover-ing completeness and accuracy of the pathology data,

pathology specimens, final pathology tables, and preliminary review draft of this NTP Technical Report were conducted. Audit procedures are presented in the reports, which are on file at the NIEHS. The audit findings were reviewed and assessed by the NTP staff so that all had been resolved or were otherwise addressed during the preparation of this Technical Report.

Result : 15-Month Interim Evaluations
Ten mice of each sex in each dose group were predesignated for interim evaluation at 15 months. There were no significant differences in absolute and relative organ weights. No treatment-related changes in hematology or clinical chemistry parameters were seen. No treatment-related neoplasms or nonneoplastic lesions were found during histopathologic examination.

Body Weights and Clinical Findings
The mean body weights of dosed male mice were similar to those of the controls throughout the studies. The mean body weights of high-dose females were from 10% to 15% lower than those of the controls from week 85 until study termination. The mean body weights of low-dose female mice were similar to those of the controls throughout the studies. Clinical findings included recumbency and tremors occurring for a short period after dosing seen in treated mice of both sexes.

Survival
The terminal survival of males and females receiving resorcinol was similar to that of the controls. By week 45 of the study, no male mice in the control and low-dose groups had died, but eight high-dose male mice had died.

Sentinel Animals
Positive titers for mouse hepatitis virus were found in sentinel animals examined at 6, 12, 18, and 24 months. However, there was no clinical or histopathologic evidence of disease.

Pathology and Statistical Analysis of Results
Administration of resorcinol by gavage to male and female B6C3F, mice for 2 years did not result in any statistically or biologically significant increased incidence in neoplastic or nonneoplastic lesions in any site.

Subcutaneous tissue: The incidence of subcutaneous sarcoma or fibroma (combined) in males occurred with a significant negative trend and the incidence was significantly lower in the high-dose group (8/50, 6/50, 1/50).

Reference : NTP Technical Report on the Toxicology and Carcinogenesis Studies of Resorcinol (CAS No. 108-46-3) in F344/N Rats and B6C3F$_1$ Mice (Gavage Studies) NIH Publication No. 91-2858

Reliability : (1) valid without restriction
14.09.2005 (1)

Species : mouse, 2-3 months of age
Sex : female
Strain : other: Sutter
Route of admin. : dermal
Exposure period : 12 weeks
Frequency of treatm. : 2 times a week
Post exposure period : No data
Doses : 0.025 ml of a 20% solution in acetone
Result : No data
Control group : yes
Method : other: one drop (adjusted to approximately 25 µl) of the test solution was applied to the back of each mouse, twice weekly, for the duration of the experiement.
Year : No data
GLP : no data

Test substance	:	no data
Remark	:	Dose group: 27 animals; control: 12 animals; 2-stage study of carcinogenesis: initiator: 75 µg DMBS dermal, then resorcinol application.
Result	:	The response was measured in three ways. First, the percentage of surviving mice bearing one or more papilloma was ascertained. Second, the total number of papillomas on all the surviving mice was counted and divided by the number of surviving mice to give the average number of papillomas per mouse. Finally, the number of mice bearing malignant tumors was determined; the latter measure was presented as the percentage of the animals surviving on the day chosen for presentation of the data, thus partially correcting for large numbers of nontumor deaths caused by toxic levels of phenols. A higher carcinoma incidence relative to the control was not observed, however, the indidence of papilloma was higher (17% of animals; control: 0%).
Reliability	:	(2) valid with restrictions
14.09.2005		(9)

Species	:	mouse
Sex	:	female
Strain	:	other: ICR/HA Swiss
Route of admin.	:	dermal
Exposure period	:	368 days
Frequency of treatm.	:	3 times/week
Post exposure period	:	No data
Doses	:	10 mg (in acetone); +/- 5 µg benzapyrene/application
Result	:	Negative
Control group	:	Yes
Method	:	no data
Year	:	No data
GLP	:	no data
Test substance	:	no data
Remark	:	50 animals/dose and control group; test of carcinogenicity of resorcinol.
Result	:	A higher tumour incidence relative to the control group was not observed at the application site.
Reliability	:	(2) valid with restrictions
14.09.2005		(130)

Species	:	mouse
Sex	:	female
Strain	:	other: ICR/HA Swiss
Route of admin.	:	dermal
Exposure period	:	449 days
Frequency of treatm.	:	3 times/week
Post exposure period	:	No data
Doses	:	10 mg/application (in acetone)
Result	:	Negative
Control group	:	Yes
Method	:	no data
Year	:	No data
GLP	:	no data
Test substance	:	no data
Remark	:	50 animals/dose and control group; 2-stage study of carcinogenesis: initiator: 150 µg benzapyrene; 14 days later: start of resorcinol application.
Result	:	A higher tumour incidence relative to the control group was not observed at the application site.
Reliability	:	(2) valid with restrictions
14.09.2005		(130)

Species	:	rabbit
Sex	:	male/female
Strain	:	New Zealand white
Route of admin.	:	dermal
Exposure period	:	180 weeks
Frequency of treatm.	:	2 times/week
Post exposure period	:	No data
Doses	:	0.02 ml of a 5, 10 or 50% solution in acetone
Result	:	Negative
Control group	:	Yes
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	No data
Remark	:	5 animals/dose; control: 9 animals
Result	:	A higher tumour incidence relative to the control group was not observed. Only those organs or tissue which showed macroscopic changes, plus the application site were examined (inner ear).
Reliability	:	(2) valid with restrictions

14.09.2005 (120)

Species	:	rat
Sex	:	male
Strain	:	Fischer 344
Route of admin.	:	oral feed
Exposure period	:	49 weeks
Frequency of treatm.	:	No data
Post exposure period	:	No data
Doses	:	0, 0.8% (approx. 400 mg/kg bw)
Result	:	No data
Control group	:	Yes
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	other TS:
Test substance	:	> 99% purity
Remark	:	Control: 10 animals; dose: 15 animals; 2-stage study of carcinogenesis: initiator: 25 mg methyl-N-amyl-nitrosamine/kg body weight i.p. for 3 weeks (once a week); then resorcinol application; 11-12 animals/dose and control group; purity >99%.
Result	:	Retarded body weight gain and higher tumour incidence: tongue papilloma ($p < 0.05$) and oesophagus carcinoma ($p < 0.01$); no increased incidence in the case of the lungs, liver, kidneys, stomach, trachea or in the nasal region.
Reliability	:	(2) valid with restrictions

14.09.2005 (140)

Species	:	rat
Sex	:	male
Strain	:	Fischer 344
Route of admin.	:	oral feed
Exposure period	:	51 weeks
Frequency of treatm.	:	No data
Post exposure period	:	No data
Doses	:	0, 0.8% (approx. 400 mg/kg bw)
Result	:	Negative
Control group	:	Yes
Method	:	No data
Year	:	No data

GLP	:	No data
Test substance	:	No data
Remark	:	Control: 10 animals; dose: 16 animals; 2-stage study of carcinogenesis: initiator: 150 mg N-methyl-N''-nitrosoguanidine/kg body weight; then resorcinol application.
Result	:	Higher tumour incidence or hyperplasia rate in the forestomach or glandular stomach relative to the control was not observed. No other organs were examined.
Reliability	:	(2) valid with restrictions

14.09.2005 (49)

Species	:	hamster
Sex	:	female
Strain	:	other: Syrian
Route of admin.	:	oral feed
Exposure period	:	20 weeks
Frequency of treatm.	:	Daily (via feed)
Post exposure period	:	No data
Doses	:	1.5%
Result	:	No data
Control group	:	Yes
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	other TS: > 99% purity
Remark	:	15 and 10 animals/substance and control group respectively; purity: >99%; 0.9% NaCl twice s.c. (two week interval), then, from week 4, 1.5% resorcinol in feed for 16 weeks; control: 0.9% NaCl twice s.c. (two week interval); then basal diet.
Result	:	Body weight development significantly raised at end of study ($p < 0.05$), relative liver weight significantly reduced ($p < 0.001$), relative pancreas weight in range of control. Pancreas, liver and gall bladder showed no signs of neoplastic changes. In the forestomach and glandular stomach, the incidence of epithelial hyperplasia was higher,but neoplastic changes (papiloma, adenoma, carcinoma) did not occur.
Reliability	:	(2) valid with restrictions

14.09.2005 (83)

Species	:	hamster
Sex	:	female
Strain	:	other: Syrian
Route of admin.	:	oral feed
Exposure period	:	20 weeks
Frequency of treatm.	:	Daily (via feed)
Post exposure period	:	No data
Doses	:	1.5%
Result	:	No data
Control group	:	Yes
Method	:	No data
Year	:	No data
GLP	:	No data
Test substance	:	other TS:
Test substance	:	Purity > 99.5%
Remark	:	2-stage study of carcinogenesis: initiator: 70 mg N-nitrobis(2-oxopropyl)amine/kg body weight twice s.c. (two week interval), then, from week 4, 1.5% resorcinol in the feed for 16 weeks. Control: initiation with N-nitrobis(2-oxopropyl)amine, then basal diet; 20 animals/substance and control group respectively; purity: >99.5%.
Result	:	Body weight development and relative liver and pancreas weights in range

of the control; lower, non-significant ($p < 0.05$) incidence of both pancreas adenomos and hyperplasia of the Ductus pancreaticus (63%) relative to control (94%); incidence of neoplastic changes in liver and gall bladder (tubercles, carcinomas, adenomas) in the range of the control. In the forestomach and glandular stomach, the incidence of epithelial hyperplasia was higher, but neoplastic changes (papiloma, adenoma, carcinoma) did not occur.

Reliability : (2) valid with restrictions
14.09.2005 (83)

5.8.1 TOXICITY TO FERTILITY

Type	:	Two generation study
Species	:	rat
Sex	:	male/female
Strain	:	Crj: CD(SD)
Route of admin.	:	drinking water
Exposure period	:	70 days prior to mating and throughout mating, gestation and lactation
Frequency of treatm.	:	continuous
Premating exposure period		
Male	:	F0: 70 days, F1: 70 days beginning at weaning
Female	:	F0: 70 days, F1: 70 days beginning at weaning
Duration of test	:	18 months
No. of generation studies	:	2
Doses	:	120, 360, 1000 and 3000 mg/l
Control group	:	yes, concurrent no treatment
NOAEL parental	:	= 3000 mg/l
Result	:	No effects on any of the reproductive parameters
Method	:	other: EPA OPPTS 870.3800 and OECD Guideline 416
Year	:	2005
GLP	:	yes
Test substance	:	Other TS:
Test substance	:	Resorcinol USP Purity at start of study >99.855% Post-study purity >99.812%
Method	:	Protocol deviations occurred during the study but were not considered to have compromised the validity or integrity of the study.
Result	:	There were no F0 or F1 parental test article-related deaths or clinical findings during the weekly detailed physical examinations. Reproductive performance (estrous cycles, mating and fertility indices, number of days between pairing and coitus, and gestation length) and parturition in the F0 and F1 animals were unaffected by the test article. Spermatogenic endpoints (mean testicular and epididymal sperm numbers and sperm production rate, motility, progressive motility and morphology) in the F0 and F1 males were unaffected by the test article. No test article-related effects were observed on F1 and F2 pup survival or the general physical condition of the pups during the pre-weaning period. No test article-related macroscopic findings, organ weight or adverse microscopic target-organ effects were observed in the F0 or F1 parental animals. In addition, no test article-related macroscopic findings or effects on organ weights were noted in the F1 or F2 pups at the scheduled necropsies; no test article-related macroscopic findings were noted for found dead F1 or F2 pups. No effects of the test article were observed on the mean days of acquisition of balanopreputial separation and vaginal patency in the F1 pups. Decreased mean cumulative body weight gains were noted in the 3000 mg/L group F0 animals during the pre-mating period (females) or the entire generation (males). There were no clear trends in mean weekly body

weight gains in these males and females; however, mean body weights were decreased by up to 6.3% in the F0 females from study day 56 through 70. Mean body weights in the 3000 mg/L group F0 females were also decreased during the first week of gestation (up to 5.5%), throughout lactation (up to 8.4%) and after the lactation period ended (6.3%). Mean body weights and body weight gains were unaffected in the 120, 360 and 1000 mg/L group F0 males and females.

Decreased mean cumulative body weight gains were noted in the 3000 mg/L group F1 males during the entire generation. While there were no clear trends for weekly mean body weight gains, mean body weights in these males were decreased by up to 7.1% during the entire generation. Mean body weights were also reduced in the 3000 mg/L group F1 females during lactation (up to 6.1%) and after the lactation period ended (up to 7.0%). Mean body weights and body weight gains were unaffected in the 120, 360 and 1000 mg/L group F1 males and females.

Decreased mean water consumption was noted for the 3000 mg/L group F0 and F1 parental animals during the pre-mating period (females) or the entire generation (males) and for the F1 pups gang-housed by litter from PND 21-28. Water consumption was also often decreased in the 1000 mg/L group males and females, although the decreases were less severe and the onset was later in the 3000 mg/L group. Mean water consumption in the 1000 mg/L group was consistently reduced compared to the control group beginning on study days 21-24; however, slight decreases were also noted inconsistently earlier in the pre-mating period. The decreased water consumption in the 1000 mg/L group continued through the first week of gestation while the decreased water consumption in the 3000 mg/L group females continued throughout gestation and lactation. The test article-related decreases in water consumption were not considered an adverse change due to the lack of associated effects on food intake and food utilization.

No statistically significant test article-related changes in the mean concentrations of T3, T4 or TSH were noted in the F0 or F1 parental animals or in the F1 or F2 pups selected for analysis (PND 4 or PND 21). The higher TSH values noted in the F0 males at the scheduled necropsy were not considered test article-related in the absence of effects on T3 or T4, organ weights or adverse macroscopic or microscopic findings. Test article-related decreased colloid within the thyroid glands of the 3000 mg/L F0 males was not considered adverse due to the lack of associated functional effects.

Test condition : Experimental outline:

Group 1, 0 mg/L, 30 males & 30 females
Group 2, 120mg/L, 30 males & 30 females
Group 3, 360mg/L, 30 males & 30 females
Group 4, 1,000mg/L, 30 males & 30 females
Group 5, 3,000mg/L, 30 males & 30 females

Exposure conditions:

F0 males and females were administered the test article drinking water formulations from study days 0-134 (129 to 135 consecutive days of exposure).

F1 males and females surviving to the scheduled necropsies were administered the test article drinking water formulations from study days 113-269 (144 to 157 consecutive days of exposure)

The offspring of the F0 and F1 generations (F1 and F2 litters, respectively) were potentially exposed to the test article in utero and through nursing

during PND 0-21. The F1 pups selected for mating (30 sex/per group) were directly administered test drinking water formulations following weaning (beginning on PND 21).

Statistical methods used:

All statistical tests were performed using appropriate computing devices or programs. Analyses were conducted using two-tailed tests (except as noted otherwise) for a minimum significance level of 5%, comparing each test article-exposed group to the control group by sex. Each mean was presented with the standard deviation (S.D.) and the number of animals (N) used to calculate the mean. Due to the different rounding conventions inherent in the types of software used, the means and standard deviations on the summary and individual tables may differ by ±1 in the last significant figure. Statistical analyses were not conducted if the number of animals was two or less. Data obtained from nongravid animals were excluded from statistical analyses following the mating period. Statistical analyses were not performed when weekly food or body weight data for one or more animals were not available because the animals remained in the lactation phase. Where applicable, the litter was used as the experimental unit.

Parental mating, fertility, conception and copulation indices were analyzed using the Chi-square test with Yates' correction factor (Hollander and Wolfe, 1999). Mean parental (weekly, gestation and lactation) and offspring body weights and body weight changes, parental food consumption and food efficiency data, parental (twice weekly, gestation and lactation) water consumption, estrous cycle lengths, pre-coital intervals, gestation lengths, former implantation sites, live litter sizes, unaccounted sites, numbers of pups born, balanopreputial separation data (day of acquisition and body weight), vaginal patency data (day of acquisition and body weight), absolute and relative (to final body and brain weight) organ weights, sperm production rates, epididymal and testicular sperm numbers, ovarian primordial follicle counts and percentages of colloid content in the thyroid gland were subjected to a parametric one-way analysis of variance (ANOVA) to determine intergroup differences (Snedecor and Cochran, 1980). If the ANOVA revealed statistically significant ($p<0.05$) intergroup variance, the two-tailed Dunnett's test (Dunnett, 1964) was used to compare the test article-exposed groups to the control group. Mean litter proportions (percent per litter) of postnatal pup survival and pup sexes at birth (percentage of males per litter), percentages of motile and progressively motile sperm, and percentages of sperm with normal morphology were subjected to the Kruskal-Wallis nonparametric ANOVA test (Kruskal and Wallis, 1952) to determine intergroup differences. If the ANOVA revealed statistically significant ($p<0.05$) intergroup variance, the two-tailed Mann-Whitney U-test (Kruskal and Wallis, 1952) was used to compare the test article-exposed groups to the control group. Histopathological findings in the test article-treated groups were compared to the control group using a one-tailed Fisher's Exact test (Steel and Torrie, 1980). Serum hormone concentration data were subjected to a parametric one-way ANOVA to determine intergroup differences as described above. If the ANOVA revealed statistically significant ($p<0.05$) intergroup variance, the one-tailed Dunnett's test was used to compare the test article-exposed groups to the control group.

Conclusion : Based on the results of this study, an exposure level of 3000 mg Resorcinol/L was considered to be the NOAEL (no-observed-adverse-effect level) for parental systemic and reproductive toxicity, as well as neonatal toxicity, when offered continuously in the drinking water to parental rats. When expressed on a body weight basis (average of F0 and F1 animals), this concentration corresponded to approximately 233 mg/kg/day for males over the entire generation, 304 mg/kg/day for females during premating and gestation and 660 mg/kg/day for females during lactation. Decreased mean water consumption was noted for the 1000

mg/L (F0 generation only) and 3000 mg/L group F0 and F1 parental animals due to the poor palatability of water containing the high concentration of Resorcinol. The test article-related decreases in water consumption were not considered adverse even in the 3000 mg/L group because of the lack of associated effects on food intake and food utilization, which indicated that homeostasis was uncompromised. However, mean cumulative body weights were decreased in the 3000 mg/L group in both sexes and generations. Thus, 3000 mg Resorcinol/L is considered to be the maximum palatable concentration for a two-generation reproduction study due to the poor palatability.

Although Resorcinol was known to be readily absorbed and eliminated, blood Resorcinol levels could be detected in some animals in the 3000 mg/L group. Decreased colloid in the thyroid histopathology, although a non-adverse effect in this study, was observed only in the 3000 mg/L group F0 males. Therefore, the effects of Resorcinol have been appropriately evaluated in this study.

Reference : WIL Research Laboratories, LLC, 1407 George Road, Ashland, OH 44805-9281 A drinking water two-generation reproductive toxicity study of resorcinol in rats.: Study Number 455003

Reliability : (1) valid without restriction
14.09.2005 (136)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	other: CD
Route of admin.	:	dermal
Exposure period	:	19 days
Frequency of treatm.	:	Days 1,4,7,10,13,16 and 19 of gestation
Duration of test	:	19 days
Doses	:	2 ml/kg
Control group	:	yes
Result	:	No embryotoxic or teratogenic effects.
Method	:	other
Year	:	1976
GLP	:	no data
Test substance	:	other TS: see remark

Test substance : Twelve hair dye composite formulations containing Resorcinol

Method : Twelve hair dye composite formulations were tested, along with one positive and three negative control groups. The dyes were obtained from commercial suppliers and are either currently used or are considered potentially useful in hair color products today. The formulations were applied topically at a dose of 2 ml/kg on days 1, 4, 7, 10, 13, 16, and 19 of gestation to groups of 20 mated Charles River CD female rats (presence of sperm in the vagina considered day 0 of gestation).
The 12 formulations tested represented the two major classes of hair color products. Three formulations (P-22, P-23, and P-24) were of the semipermanent type that consist of preformed pigments that are deposited on the hair shaft from solvent-detergent bases. The nine remaining formulations were of the type that result in the oxidation of colorless intermediates, which are deposited as colored polymers in the hair shaft. These oxidation formulas have an ammoniacal soap base and are mixed with an equal volume of 6% hydrogen peroxide just prior to use.
The hair at the site of application on the dorso-scapular area was shaved closely the day before the solutions were applied. The negative control animals were untreated but were shaved. Three separate and discrete negative control groups were maintained in order to determine the degree

of variability among small groups of control animals and to utilize this information in assessing treatment effects.
The positive control group received acetylsalicylic acid by gavage at a dose of 250 mg/kg on days 6 through 16 of gestation. Although some compounds have been reported to be teratogenic by topical application, it was felt that their teratogenic-toxic dose relationship had not been that well defined and that the real purpose of a positive control in a test such as this was served by the oral administration of the salicylate.
The mated females were housed individually in temperature- and humidity-controlled rooms during the study and were weighed on, the days the dyes were administered. Ralston Purina Laboratory Chow and water were available ad libitum

Statistical methods:
All statistical analyses compared the treatment groups with the control groups. The number of females exhibiting resorption sites, number of females exhibiting two or more resorptions, number of dead or resorbed fetuses, and the number of fetuses with soft-tissue or skeletal anomalies and accessory ribs was compared using chi-square test criterion with Yates' correction on 2 X 2 contingency tables as described by Steel and Torrie (1960) or Fisher's exact probability test (Siegel, 1956) as appropriate to judge the significance of difference.
The mean number of corpora lutea, implantation sites, live fetuses, and resorption sites was compared by analysis of variance (one-way classification) as described by Steel and Torrie (1960) using Dunnett's (1964) multiple comparison tables to judge the significance of differences.
The live fetal weights were compared by analysis of variance (hierarchal classification) as described by Steel and Torrie (1960) using Dunnett's (1964) multiple comparison tables to judge the significance of differences.
Statistically significant differences between groups were judged valid only when there were significant differences between any one of the dye treated groups and each of the three untreated control groups.

Result : No signs of toxicity were seen throughout the study. Except for the changes in the color of the skin and hair at the site of dye application, no irritation or other changes in appearance were seen.
Changes in female body weights were similar for rats in the untreated controls and all dye-treated groups. A marked reduction in maternal weight gain through gestation was observed in the rats receiving acetyl-salicylic acid as compared with either the untreated control rats or dye-treated rats.
Mean food consumption for all groups throughout gestation was similar except for rats in the acetylsalicylic acid group; these rats showed a moderate decrease in food consumption from days 7 to 13 of gestation. This decrease was not seen from days 13 to 20 of gestation.
The dye formulations produced no significant differences in the mean number of corpora lutea, implantation sites and live fetuses, and the sex ratio when compared with the untreated control groups. No differences between groups were seen regarding the number of females exhibiting resorption sites or mean resorptions per pregnancy. No significant changes were observed regarding soft-tissue anomalies between the dye-treated groups and the untreated control groups. Normally occurring skeletal variations were present in all groups; the most frequent variation noted was accessory ribs.
A statistically significant increase in skeletal anomalies appeared in the group receiving formulation 7402. Nine fetuses of the 169 examined revealed anomalies that are regarded as minor skeletal changes. Seven of the nine fetuses displayed notched ribs and two displayed short ribs. These minor skeletal changes were seen in only 3 of 20 litters examined and are not regarded as biologically significant.
The results observed in the positive control group, namely an increase in embryotoxicity (e.g., increase in teratogenicity, increase in embryo death, and decrease in fetal weight), are in accord with the literature concerning the effects of aspirin upon fetal rat development (Kimmel and Wilson, 1973;

Kimmel et al., 1971; McColl et al., 1965).

Test condition : Three negative controls were used and a positive control of acetylsalicylic acid.
20 mated Charles River CD females were dosed. Age at start of study is unknown.

Twenty pregnant rats from each group were sacrificed on day 20 of gestation by chloroform anesthesia, and Cesarean sections were performed. The uteri were examined, corpora lutea of pregnancy counted, and the number, distribution, and location of live, dead, and resorbed fetuses recorded. All fetuses were examined for gross anomalies, sexed, and weighed. Approximately one-third the fetuses from each litter were fixed in Bouin's solution and subsequently examined for visceral anomalies by razor blade sectioning (Wilson and Warkany, 1965). The remaining fetuses in each litter were fixed in 95% ethyl alcohol, eviscerated, cleared, stained with KOH-alizarin red S (Staples and Schnell, 1964), and examined for skeletal anomalies. Fetal examinations were performed in a random order with treatment group identity unknown to the examiner.

Conclusion : From this investigation, the administration of Resorcinol every third day of the gestation period produces no embryotoxic or teratogenic effects.

Reference : Burnett et al. Journal of Toxicology and Environmental Health, 1:1027-1040, 1976

Reliability : (2) valid with restrictions
12.09.2005 (15)

Species : rat
Sex : female
Strain : No data
Route of admin. : oral unspecified
Exposure period : 6-15 day of gestation
Frequency of treatm. : Daily
Duration of test : 10 days
Doses : 40, 80, 250 mg/kg bw
Control group : No data
Result : No embryotoxic or teratogenic effects

Remark : 23 dams/dose; no detailed information of the maximum tolerable range.
Reliability : (2) valid with restrictions
14.09.2005 (46)

Species : rat
Sex : female
Strain : Sprague-Dawley
Route of admin. : oral unspecified
Exposure period : 6-15 days of gestation
Frequency of treatm. : daily
Duration of test : 10 days
Doses : 125, 250, 500 mg/kg bw
Control group : yes
Result : No embryotoxic, foetotoxic or teratogenic effects
Method : other
Year : 1985
GLP : no data
Test substance : other TS: see remark

Test substance : Resorcinol (Lot No. 21005013) was obtained from Lowenstein Dyes, Cosmetics, Inc., Brooklyn, New York.

Method : Following acclimation, each male was caged with two females. Day 0 of gestation was defined as the day on which a copulatory plug or the presence of sperm in a vaginal smear was detected. Following mating, each female was separately housed.
Ten to thirteen pregnant females were assigned on a random basis to

resorcinol.
The doses were 125, 250, and 500 mg/kg for resorcinol. The dyes were dissolved in propylene glycol and administered by gavage to the dams on Days 6 to 15 of gestation.
Doses were determined from previous maximum tolerated dosage (MTD) studies performed on five non-pregnant female Sprague-Dawley rats per dose, weighing between 200 and 225 g for each compound. The dose which produced no more than a 10% reduction in body weight after 10 consecutive administrations at 10 ml/kg, or the highest concentration which did not produce mortality if a weight reduction could not be obtained was deemed the MTD and selected as the high-dosage group for the study. Intermediate- and low-dosage groups were obtained by dividing the MTD by a factor of approximately 2 and 4, respectively.
Solutions were prepared fresh daily and administered at 10 ml/kg. Each of the dyes was evaluated individually with each study containing a concurrent vehicle control, propylene glycol, which was administered at 10 mg/kg in the same manner as described above. Dams were observed daily throughout gestation for general health and condition and were weighed to the nearest gram on Days 0, 6, 16, and 20 of gestation.
A positive control, vitamin A (Aquasol A Drops, USV Laboratories, N.Y.) was included. Vitamin A was administered in a single po dose (100,000 IU/rat) on Day 9 of gestation.
On Day 20 of gestation, estimated as 24 hr before parturition, dams were killed by carbon dioxide inhalation. The abdominal wall was incised longitudinally and both uterine horns were exposed. The viability of each fetus was determined. The metrial glands were counted, identifying original implantation sites. An implantation site not occupied by a fetus was designated a resorption site. Each fetus was sexed and weighed to the nearest 0.1 g. Any external fetal malformations were recorded.
One-half of the fetuses were randomly selected from each litter and placed in Bouin's fixative for subsequent visceral examination according to Wilson's procedure (1965). The remaining half of the fetuses were eviscerated, fixed in 95% isopropyl alcohol, macerated in 2% potassium hydroxide, and stained with 0.5% potassium hydroxide and alizarin red S (Dawson, 1926) for skeletal evaluation.

Statistical Methods:
Mean number of corpora lutea, total implantations, viable fetuses, mean fetal body weight, and mean maternal body weight gain were analyzed by Student's t test (Hoover, 1970). The number of abnormal fetuses were compared by chi-square analysis (Wart and Neidt, 1954) and resorption were standardized to litter by Wilcoxon-Mann-Whitney u test (Siegel, 1956). Probability for all statistical analyses was at the 0.05 level.

Remark : 13 dams/dose; high dose lay in the maximum tolerable range.

Result : Resorcinol did not produce a significant decrease in mean maternal weight gain at the high doses utilized, although a reduction was observed. No additional significant differences were observed in the incidence of fetuses with gross, visceral, or skeletal anomalies or any of the other parameters investigated.
Vitamin A, the positive control, was teratogenic, producing a significant increase in the number of abnormal fetuses. Frequency of anomalies ranged from 28 to 95% with major anomalies including hydrocephaly, exencephaly, prognathia, macroglossia, open eye, microphthalmia, cleft palate, hydronephrosis, and agenesis of skull bones.

Test condition : Male and female Sprague-Dawley rats (Charles River, Wilmington, Mass.) weighing 225 to 250 g were acclimated for 2 weeks under standard laboratory conditions (50 ± 10% relative humidity, 21 ± 2°C, and 12-hr light cycle). Rodent feed (Purina Laboratory Rodent Chow, Ralston Purina Co., Inc., St. Louis, Mo.) and water were available ad libitum.

Conclusion : Resorcinol did not produce teratogenic effects.

Reference : Dinardo et al. (1985): Toxicol. Appl. Pharmacol. 78, 163-166.

Reliability	:	(2) valid with restrictions
14.09.2005		(28)
Species	:	rabbit
Sex	:	female
Strain	:	No data
Route of admin.	:	oral unspecified
Exposure period	:	6-18 day of gestation
Frequency of treatm.	:	Daily
Duration of test	:	13 days
Doses	:	25, 50, 100 mg/kg bw
Control group	:	yes
Result	:	No embryototoxic, foetotoxic or teratogenic effects
Remark	:	18-26 dams/dose; no detailed information of the maximum tolerable range.
Reliability	:	(2) valid with restrictions
14.09.2005		(46)
Species	:	hen
Sex	:	No data
Strain	:	other: White Leghorn chick eggs
Route of admin.	:	other: applied to inner shell membrane
Exposure period	:	Single
Frequency of treatm.	:	only once
Duration of test	:	1 day
Doses	:	99, 198, 396, 804, µg/chick egg
Control group	:	yes
Remark	:	5 µl of resorcinol (in acetone)/chicken egg were applied to the inner shell membrane of 3 day old chick embryos. 20-30 chick eggs/dose group; 10 chick eggs/controlgroup (vehicle).
Result	:	Dose at which 50% of embryo died and/or malformed: ED50=264.3 µg/egg; dose at which 50% of the embryo died: LD50=297.3 µg/egg; external signs of malformation include: open coelom, wing and leg defects, oedema or lymph vesicles.
Reliability	:	(2) valid with restrictions
14.09.2005		(71)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

Type of experience	:	Human
Method	:	Method followed was that developed by Feldmann and Maibach for measurement of percutaneous adsorption in man. This method involves quantifying absorption on the basis of the percentage of radioactivity excreted in the urine following application of a known amount of labeled compound.
Test substance	:	Commercially available hair dye product, representatives of permanent (Nice'n easy)
Remark	:	In three probands, dermal adsorption of resorcinol through the use of hair dyes was investigated. Hair dyes that contained radioactive labelled resorcinol were distrubuted through the hair and over the scalp in

accordance with instructions for use. After an exposure time of 25-28 min, the hair was rinsed, dried and cut off in order to prevent further adsorption. Excretion of the radioactivity via the urine was then monitored for 144 h max (collection initially after 4 h later 24 h): a total of 0.076% of the applied radioactivity was excreted via the urine. A half life time for elimination via the urine was calculated as being T1/2 = 31h. From data for elimination of the radioactivity via the urine after 24 h, an absorption rate of 2.2 x 120E-10 mol/cm2 x h (0.024 µg/cm2 x h) was calculated. When the test for elimination was also 31 h and a total of 0.177% of the applied radioactivity was excreted via the urine within 7 days.

Reference : Wolfram (1985): Dermatol. 6, 409-422

13.09.2005 (139)

5.11 ADDITIONAL REMARKS

Type : Immunotoxicity

Remark : Cell incubated with 1.1-11.0 µg resorcinol/ml for 2 days at 37°C

Result : Formulation of specific antibodies (IgM) in human-human hybrid HB4C5 cells was inhibite as a function of concentration. the relative growth rate (cell proliferation) diminished as a function of concentration.

09.12.2003 (79)

Type : other: Nitrosation in vitro

Remark : Nitrosation of 10 mM proline in vitro (pH 2-5; 37°C, test duration: 15 minutes) was catalyzed as a functionof pH by 1 mM resorcinol (approx. 110 µg/ml)

Result : The optimum pH value for N-nitrosation was 2.5. The maximum catalytic effect exerted by resorcinol was, however, produced at a pH of 4, at which there was a 26 fold increase in the N-nitroproline formation compared to the control.

09.12.2003 (99)

Type : other: Nitrosation in vitro

Result : In BD VI rats, oral application by gavage of 1 and 5 µmol resorcinol/animal (110 and 551 µg/animal respectively) led to increased formation of N-nitrosoproline relative to control (administration of proline only). Excretion of N-nitrosoproline via the urine within 24h of application increased as a function of concentration approx. 7 fold and 9 fold respectively.

12.11.2003 (99)

Type : other: kinetics

Remark : In the rat, resorcinol absorbed via the skin or the G.I tract. 90% of orally administered doses are excreted again within 24 h via the urine: 3% via the faeces, and 0.1% exhaled as CO2. 50% of the dose excreted via the bile enters the enterohepatic circulation. More than 70% of the resorcinol excreted via the urine is present as the glucuronide or sulphate conjugate, with less tha 5% present as free resorcinol. Repeated administration over 30d did not lead to storage or accumulation in tissues. The half-life time for elimination from plasma following subcutaneous application lay beteen 8.6 and 10.5 h. In humans, the adsorption rate via the skin was 0.37 µg/cm2/h. Also in humans the resorcinol excreted via the urine following dermal application (12 mg/kg body weight/day for 4 weeks (see section 5) is in the form of the glucuronide or the sulphate conjugate. No resorcinol could be detected in the blood.

20.05.2004 (12) (26) (40) (70) (88) (104) (141) (142)

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

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10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT